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MESODERMAL MIXED TUMOURS OF THE FEMALE GENITAL TRACT*

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MR. President, Ladies and Gentlemen. I am deeply conscious of the honour of being chosen to deliver this year's Blair Bell Memorial Lecture. The work of William Blair Bell is known to pathologists as well as to clinicians, particularly his interest in the problem of malignant disease.

Due to improvements in surgical, radiotherapeutic, anaesthetic and diagnostic techniques, combined with chemotherapy, antibiotics and intravenous transfusions, more patients suffering from malignant disease are being treated. This progress has been paralleled by increased facilities for adequate examination of pathological material. Study of so-called rare tumours has therefore become easier and more important.

Mesodermal mixed tumours of the female genital tract arise almost exclusively from the mucosa of the body of the uterus, cervix and vagina. They are alluded to as mixed tumours because they may contain tissues heterotopic to the location in which they are found. A variety of tissues is encountered but the tumours are monodermal in origin and are not to be confused with teratoma (Nicholson, 1956). Many names have been applied to them depending on the site of origin, naked eye appearance, histological structure or suggested histogenesis—examples are Botryoid sarcoma, Chondrosarcoma, Rhabdomyosarcoma, Mesenchymoma, Carcino-sarcoma and Dysontogenetic or Müllerian tumours. There seems to be need of a generally acceptable title; that suggested by Kehrer (1906), "mesodermal mixed tumour", is preferred and has been accepted by Meikle (1936) and by Thiery and Brunschwig (1955). Wilfred Shaw (1928) wrote, "the modern tendency has been to collect these tumours together under the name 'Mixed Tumours'". Unfortunately his trust in a modern tendency was unfounded and the plea for classification as a composite group is still relevant.

There are many reviews of the literature. In most instances the articles refer to tumours of either corpus, cervix or vagina or to a particular histological feature so that a comprehensive review is difficult to obtain. Attention is drawn to the papers of Shaw (1928), MacFarland (1935), Meikle (1936), Amolsch (1939), Liebow and Tennant (1941), Lebowich and Ehrlich (1941), Glass and Goldsmith (1941), Hill and Miller (1951), Klein (1953), Sternberg, Clark and Smith (1954), Thiery and Brunschwig (1955) and Karpas and Speer (1957). Reports date from those of Wagner (1854) and Guersant (1854); the early literature is reviewed by Wilms (1899).

Early British contributors are Heckford (1869) (Fig. 1), Marsh (1874), Galabin (1886), D'Arcy Power (1895), Reid (1902), Williamson (1905), Boyd (1905), McCann (1908), Glynn and Blair Bell (1914), Murray and Littler (1914) and Nicholson (1918).

* William Blair Bell Lecture, 1957.

FIG. 1

Illustration in the case report of Heckford (1869). The tumour mass distends and projects from the vagina of an infant. Anterior view. A.—Uterus and ovaries. B.—Abdominal wall. C.—Section of bladder. D.—Vagina and protruding vegetations. E.—Rectum. F.—Sac.

INCIDENCE

Reviewers differ greatly in the number of cases they accept. Thiery and Brunschwig consider that less than 130 are authentic; to this figure they add 11 but do not include the 21 reported by Sternberg *et al.* These two additional series relate to surgical material from individual hospitals and indicate that mesodermal mixed tumours of the female genital tract are more frequent than has previously been contended.

Personal experience is in agreement with this view. In the last 10 years, 20 patients suffering from mesodermal mixed tumours of the uterus have been operated upon at the Women's Hospital, Birmingham. Specimens from a further 20 treated at other hospitals have been submitted for opinion to the Pathology Department during the same time. From this series, figures indicating the incidence of the disease are of doubtful value but we conclude that the tumours are not exceedingly rare. Sternberg *et al.* find the incidence in the uterus to be "about the same frequency as leiomyosarcoma of the uterus". The records of the Women's Hospital, Birmingham, contain 37 instances of uterine sarcoma during the 10 years in which 20 cases of mesodermal mixed tumours were diagnosed.

To justify the claim that mesodermal mixed tumours of the female genital tract are a composite group, it is necessary to study the features that have caused them to be classified in subgroups.

BOTRYOID SARCOMA

This term—suggested by Pfannenstiel (1892)—refers to naked eye resemblance of the polypoid tumour masses to a bunch of grapes. Tumours of this type are the earliest recorded and comprise most of the reports reviewed by Wilms. Not all grape-like tumours, however, show similar histology any more than those having similar histological structure are all grape-like.

Botryoid tumours are said to arise from the vulva and vagina in infancy, from the cervix in adolescence and from the body of the uterus after the menopause. This generalization may be true if study is limited to naked eye observation, although even then there are exceptions. Whether the polypoid masses arise from corpus, cervix or vagina, they sometimes present at the vulva. Several cases ascribed to vaginal origin are doubtful—Shaw (1928) and Duncan and Fahmy (1953) mention the difficulty of demonstrating precise origin in museum specimens of infantile organs. Cervical botryoid growths tend to fill the vagina and appear to grow there: in some instances the tumours arise from both cervix and vagina. Corporeal mesodermal mixed tumours rarely assume a botryoid appearance although histologically they may be identical with those of the lower portions of the genital tract. Mechanical factors in part determine the shape, size and consistency of the neoplasms.

A tumour may first be seen as a polyp either of the vulva, in the vagina or on the cervix and is sometimes wrongly considered benign even on histological examination. This is stressed by Maslen Jones (1928), Amolsch (1939), Ferreira (1951), Duncan and Fahmy (1953), Creadick (1954) and by others. In children the occurrence of such polyps is always suspicious although James (1951) has reported a benign polyp of the cervix in a child aged 3 years. Heterotopic elements are demonstrated less frequently in young patients and cartilage is probably never seen in the grape-like tumours of infancy: to exclude such instances from the group of mesodermal mixed tumours appears an arbitrary decision.

In the present series of 40 cases, 7 of the tumours could be classified as botryoid in type. The site of origin related to age of the patients is:

Vaginal (2): both at 3 years.

Cervical (4): 7 months, 20, 38 and 48 years.

Corporeal (1): 65 years.

Attention is particularly drawn to the occurrence of a typical growth arising from the cervix of a 7-months infant (Fig. 2). Portions of this tumour first showed at the vulva as in the patient aged 20 years (Figs. 3 and 4) and in the 2 instances of vaginal growth. Histological examination of the grape-like tumours in this series shows myxosarcoma with clusters of embryonic cells (Figs. 5 and 6). Heterotopic tissues (cartilage and/or cross-striated muscle fibres) are present in 5 of the 7 tumours; the 2 in which heterotopia has not been demonstrated are from children aged 7 months and 3 years respectively. For the most part the polypoid processes are covered by stratified squamous epithelium which in some instances shows atypical hyperplasia (Fig. 7). A diagnosis of benign polyp was originally made in 2 of the cases. In one patient, aged 3 years, the polyp appeared at the vulva and was ligated: the lesion recurred and eventually the vagina was found to be filled with masses of inoperable growth. In the other patient, aged 38 years, a cervical polyp, reported histologically as benign, had been excised 16 month before her attendance at a local hospital: examination now revealed a cluster of polyps arising from the cervix and biopsy of these showed characteristic mesodermal mixed tumour containing foci of cartilage. Review of the section of the original polyp revealed a myxomatous structure containing small clusters of embryonic cells but no heterotopic tissues.

Infiltration of the fibromuscular wall of the cervix is not easily demonstrated in the specimens examined but in one skeletal muscle fibres were found deep in the substance. Cervical and vaginal mucosa intervening between the polypoid tumour masses appears relatively normal. The neoplasm appears to arise in multi-focal form.

Corporeal Mesodermal Mixed Tumours

Mixed tumours arising in the corpus uteri are rarely mentioned in early records. The earliest is that of Anderson-Edmansson (1870) but Wilms' review (1899) refers almost entirely to tumours of the cervix, vagina and lower urinary tract. Meikle (1936) was able to find records of 45 corporeal tumours compared to 31 cervical: Glass and Goldsmith (1941) increase the figures to 58 and 36 respectively. Hardy and Moragues (1952) bring the total of reported corporeal mixed tumours to 116. In the present series there were 26 tumours of the corpus compared with 14 of the cervix and vagina. These tumours are usually observed in patients after the menopause. An interesting exception in the present series is the occurrence in a patient 15 years of age: polypoid growth arising from the endometrium at the fundus brought about inversion of the uterus. This case is to be reported in full in a separate contribution.

In the body of the uterus, grape-like tumours are rare but a polypoid form of growth is nevertheless characteristic (Figs. 8, 9 and 10). Origin is from the endometrium, more commonly from the posterior wall and upper half of the uterus. The tumour mass may be single but sometimes multiple growths occur—Nicholson (1918) gives a classical description of the multiple form. In comparison with botryoid growths the corporeal tumours are generally firm, opaque and individually may reach several centimetres in diameter. The surface of a tumour is usually smooth and lobulated but may be ulcerated. Haemorrhage and necrosis often destroy the

compact polypoid appearance. The base of a tumour may be broad or the growth be pedunculated. Demarcation from the underlying myometrium is usually distinct but in advanced disease infiltration may occur. Continued growth results in enlargement of the polypoid masses which distend the cavity of the uterus, dilate the cervical canal and frequently project into the vagina (Fig. 11). Bisection of a tumour shows a soft, greyish-white or pink moist surface: there is rarely any special feature to distinguish it from uterine sarcoma.

The endometrium adjacent to a tumour shows no characteristic feature. Fibromyomata are often present in a uterus the seat of mesodermal mixed tumour but there is no evidence to suggest a causal relationship. Their presence, however, may lead to the wrong assumption that a soft polypoid mass in the cavity of the uterus is malignant change in a submucous fibroid (Fig. 12).

Histological examination of corporeal mesodermal mixed tumours usually shows embryonic sarcoma containing glandular epithelium, benign or malignant. In the present series of 26 corporeal tumours, an admixture of sarcoma and carcinoma is present in 14; heterotopic structures are found in 16—cross-striated muscle, 9, cartilage, 5, and osteoid tissue, 3.

Rhabdomyomatous Component

The presence of rhabdomyomatous components in a neoplasm is always of great interest in pathology. In tumours of the female genital tract striated muscle is generally acknowledged to be heterotopic. The paper of Robertson (1909) details 10 cases of uterine rhabdomyosarcoma and it is pertinent to this lecture to point out that the first specimen demonstrated in this country was by Blair Bell (1912), subsequently fully reported by Glynn and Blair Bell (1914). Credit is sometimes given to D'Arcy Power (1895) but the rhabdomyomatous component of the tumour was not demonstrated until Wilfred Shaw re-examined the preserved specimen. The paper of Glynn and Blair Bell remains a classic. Two cases are described; tissue was passed *per vaginam* by each patient, aged 62 and 75 years respectively. The operation specimens revealed polypoid growth in the uterine cavity arising from the posterior wall. Cross-striated muscle fibres were present in each tumour—in one, only in the portion passed before operation. The authors draw particular attention to embryonic cells which they call "Sarcoblasts" and we now may call rhabdomyoblasts (Fig. 13). They describe these large cells in detail and recognize that in this embryonic form cross-striations may not be demonstrable. Fifteen previous cases are reviewed and the finding of a variety of tissues is listed:

Sarcoblasts	5
Myxomatous tissue	7
Cartilage	5
Gland tissue	6

This glandular epithelium may be benign or malignant.

Some authorities (Lebowich and Ehrlich, 1941; McElin and Davis, 1952) consider that the demonstration of cross-striated muscle cells is essential for the diagnosis of mesodermal mixed tumours of the genital tract. Such demonstration is certainly satisfying and must be attempted. It often requires painstaking search even by oil immersion lens (Symmonds and Dockerty, 1955) and is best brought about by the use of Heidenhain's iron haematoxylin with very careful differentiation (Cappell and Montgomery, 1937). The paper of Glynn and Blair Bell, however, shows that recognition of the mixed nature of the tumour can be made in the absence of cellular cross-striation. Rhabdomyoblasts are heterotopic structures and their presence in embryonic sarcoma containing epithelial elements and sometimes cartilage is sufficient for diagnosis. Rhabdomyoblasts are characteristically rounded cells measuring 20–30 μ in diameter. Their cytoplasm is strongly acidophilic in staining reaction and slightly granular; the nuclei, usually eccentric in site, show a sharp, darkly staining border and contain clumps of chromatin (Fig. 14). The cells are sometimes oval or elongated and terms such as "ribbon or strap cells, tennis-racket cells" have been applied; the cytoplasm of these misshapen cells is often extensively vacuolated. The immature muscle cells may be in large numbers in one portion of a section and few in other portions. The various features are

beautifully illustrated in the paper by Kulka and Douglas (1952). The frequency with which cross-striations are demonstrated will depend on the degree of cellular differentiation, the staining technique and the time taken in searching.

Well-developed cross-striation of muscle cells and fibres was found in 13 of the 40 cases in this series (Figs. 15 and 16). Faint striations were present in other cases, sometimes in rhabdomyoblasts but these embryonic cells are best recognized from their general characteristics in sections stained by haematoxylin and eosin.

Cartilaginous Component

Cartilage is another heterotopic tissue found in genital mesodermal tumours. It has been demonstrated in the endometrium (Aabye, 1955) but the source in these instances is open to question. Cartilage is formed by metaplasia in the stroma of many tumours but in those under discussion arises from the parenchyma. It is not found in genital mesodermal tumours of infants but in older patients may form the main bulk. Such tumours have been labelled "chondrosarcoma": Hartfall (1931) reports 3 such cases and reviews the literature. Cartilage is usually sporadically distributed and on histological examination is seen as islands of well-formed or embryonic cells (Fig. 17). There is considerable variation in the frequency with which cartilage is recorded as a component. Liebow and Tennant (1941) quote its presence in 42 of 65 cases: Glass and Goldsmith (1941) give an incidence of 60 per cent in 94 cases whereas Symmonds and Dockerty find it only once in 19 specimens. Personal experience suggests that cartilage is more frequent in tumours of the cervix than of the body of the uterus—it was found in 3 of 6 botryoid tumours of the cervix and vagina and in 5 of 26 corporeal tumours. In one instance an island of cartilage was found in small portions of growth removed by curettage but none was encountered in many blocks of tissue from the subsequently removed corporeal neoplasm.

Osteoid tissue may be formed by metaplasia in the stroma of a tumour. The presence of such tissue in a mesodermal tumour is difficult to evaluate but in some instances it appears to be evidence of heteroplasia by the tumour cells. Glass and Goldsmith state that the development of osteogenic sarcoma has been recorded. The finding of osteoid tissue in a malignant growth of the genital tract is not diagnostic of mixed tumour but indicates that search for further evidence is worth while.

Smooth muscle fibres have been demonstrated in mesodermal mixed tumours (Nicholson, 1918; Glass and Goldsmith, 1941). They are seen particularly in more differentiated tumours but are difficult to identify in anaplastic growths.

Adipose tissue has also been demonstrated (Nicholson) and is evidence of heteroplasia. In most instances it is difficult to distinguish between fat-producing cells and degenerate fat-containing cells.

Lymphomatous elements are discussed by Sternberg *et al.* (1954).

Other heterotopic tissues have been recorded but their presence may indicate teratomatous origin rather than that under discussion.

Sarcomatous Component

The constant and main component of mesodermal mixed tumours is some form of sarcoma. In botryoid tumours the sarcoma is predominantly of myxomatous type and may be mistaken for myxomatous degeneration of benign connective tissue. In these instances there is usually evidence of abnormal nuclear activity if sufficient material can be examined. Firm tumours arising from corpus or cervix uteri may show myxosarcoma on histological examination but are more likely to be cellular and pleomorphic. Most examples of mesodermal tumours contain areas of embryonic sarcoma with clusters of undifferentiated cells lying in loose fibrillary tissue. A mixture of cellular, myxomatous and embryonic forms of sarcoma is usual, the variation in pattern often suggesting the nature of the neoplasm. Differentiation into the specific types, rhabdomyosarcoma and chondrosarcoma, has already been mentioned.

The tumour frequently confused with uterine mesodermal tumour is endometrial sarcoma. McElin and Davis (1952) regard mesodermal tumour as a variant of endometrial sarcoma. Sternberg *et al.* (1954) consider that endometrial sarcoma constitutes the major portion of the

sarcomatous component in mesodermal mixed tumours. Symmonds and Dockerty (1955) review 43 cases classified as endometrial sarcoma at the Mayo Clinic; of these they label 19 as mesodermal mixed tumours and 7 as carcinosarcoma. Personal experience suggests that pure endometrial sarcoma is a very rare tumour; polypoid sarcomatous growths arising from the genital mucosa are more likely to be of mixed type. Distinction is not always possible; demonstration of heterotopic tissues signifies mesodermal mixed tumour but in undifferentiated neoplasms these tissues are not present. An occasional endometrial gland may persist in endometrial sarcoma but the presence of actively proliferating glandular epithelium in the substance suggests that the tumour has the property of primitive Müllerian mesoderm to give rise to epithelium and stroma and is of mixed mesodermal type. When mesodermal mixed tumours invade the myometrium, the sarcomatous component may be mistaken for Stromal Endometriosis or so-called "Malignant Stromatosis" (Fig. 18). The characters of this lesion are described by Hunter, Nohlgren and Lancefield (1956).

Many examples of mesodermal mixed tumour of the uterus are recorded under the term "Uterine Sarcoma" and may be lost to the reviewer. Articles which include specific cases are those of Novak and Anderson (1937), MacFarlane (1950). Thornton and Carter (1951), Herman and Barrows (1955) and Webb (1955). An interesting paper is that of Schiffer, Mackles and Wolfe (1955) concerning re-appraisal of 49 tumours originally diagnosed as uterine sarcoma; 5 are re-classified as mixed mesenchymal, 3 as carcino-sarcoma and 1 as rhabdomyosarcoma. Histological review of similar series would probably yield comparable results.

Sarcomatous development in fibromyomata, especially of submucous type, may be confused with mesodermal mixed tumour. In some instances the patterning of uterine leiomyosarcoma is characteristic and resembles muscle bundles but in others cellular pleomorphism obscures the origin from fibromyoma. In these the myxomatous and embryonic appearance of mesodermal mixed tumour is usually lacking and there are no epithelial or heterotopic elements. The article by Diehl and Haught (1946) on vaginal sarcoma includes examples of mesodermal mixed tumours.

Epithelial Component

Mesodermal mixed tumours are usually ensheathed by epithelium, stratified squamous in cervical and vaginal growths and usually columnar in corporeal neoplasms. Lack of ulceration is often surprising. Study suggests that the surface epithelium undergoes active proliferation to keep pace with the rapidly growing tumour substance. The epithelium dips into folds in and between tumour masses and frequently shows abnormal hyperplasia (Figs. 19 and 20). In corporeal tumours epithelium is generally present in the substance; it may be in the form of glands and tubules but frequently is hyperplastic or carcinomatous. The epithelial proliferation appears to be an integral part of the neoplastic process.

We recall that Glynn and Blair Bell (1914) noted gland tissue—benign or malignant—in 6 of 17 cases; Leith Murray and Littler (1914) report an adeno-chondro-sarcoma. Glass and Goldsmith (1941) find an epithelial component in 57 per cent of 94 cases they review, Symmonds and Dockerty (1955) in 14 of their 19 cases and Thiery and Brunschwig (1955) in 10 of 11. A striking report is that of Sternberg *et al.* (1954), who find carcinoma in 19 of their 21 specimens of mesodermal mixed tumours.

Carcino-Sarcoma

The presence of carcinoma and sarcoma in the same tumour is often referred to as carcino-sarcoma—a term "often loosely and incorrectly applied" (Novak, 1952a). Full discussion regarding carcino-sarcoma in general is outside the scope of this paper—the reader is referred to the articles of Harvey and Hamilton (1935) and Saphir and Vass (1938). We are concerned, however, with the significance of so-called carcino-sarcoma in relation to mesodermal mixed tumours (Karpas and Speer, 1957).

Robert Meyer (1912) divides tumours containing both sarcoma and carcinoma into three categories: "Collision tumour" refers to an admixture following union of separate sarcoma

and carcinoma; "Combination tumour" occurs when the stroma of a carcinoma undergoes sarcomatous change—this is best known in transplantable tumours of animals; "Composition tumour" refers to malignant transformation of epithelial and connective tissue elements in the same growth. This third group is referable to the mesodermal mixed tumours under discussion but care must be taken to exclude specimens of the other two categories. Nicholson (1956) defines a composition tumour as "two kinds of growth situated in and arising from the same spot" and Novak (1952b) as "sarcoma and carcinoma arising from the same stem cells".

Mesodermal mixed tumours, especially those arising in the body of the uterus, often show "composition carcino-sarcoma". There is little justification, however, for regarding these as a special group of neoplasms. The demonstration of heterotopic structures is as frequent and as difficult in these as in other forms of mesodermal mixed tumour. There is no general difference between the histological appearance of tumours that contain heterotopic tissues and those that do not. Distinction based solely on the presence or absence of such tissues is arbitrary and possibly incorrect. We recall that, in one of the cases of Glynn and Blair Bell (1914), cross-striations were only found in a portion of tissue passed *per vaginam* and we have instanced the finding of cartilage in curetted material but not in the main tumour mass. The statement of Hardy and Moragues (1952) is worth repeating: "In our experience it seems hardly reasonable when one encounters a tumour of the uterus which is made up of manifestly heterotopic elements and which follows a characteristic clinical course, to exclude it simply because one is unable to demonstrate a certain type of embryonal cell which all authors are agreed may easily be overlooked and whose demonstration requires extreme diligence, highly specialized staining techniques and very probably a liberal portion of just ordinary good fortune."

In the present series of 40 tumours, there are 17 examples of an admixture of carcinoma and sarcoma of composition type—5 are cervical in situation and 12 corporeal. Obvious heterotopic tissues are present in 6—cartilage 3, cross-striated cells 3—and rhabdomyoblasts are seen in a further 8. In many instances the carcinoma is of glandular type but in some there is squamous cell carcinoma and in others both adenocarcinoma and squamous cell carcinoma. Aberrant epithelium in cords, tubules and glands is often present in addition to carcinoma. These various components occur as islands in the midst of embryonic sarcoma or as masses of malignant growth merging into sarcoma and quite often it is impossible to distinguish between fields of sarcoma and carcinoma (Figs. 21, 22 and 23). Silver impregnation stains for reticulin are unhelpful in such admixture and are only clear when the malignant growths can be distinguished in their patterning by the usual staining techniques. In some examples areas of malignant tissue are reminiscent of granulosa-cell tumour (Fig. 24) and may account for the occasional reports of this tumour in the uterus (Morehead and Bowman, 1945; Langley, Smith and Woodcock, 1953).

The epithelial component as well as sarcoma is sometimes present in metastases (Glynn and Blair Bell, 1914; Nicholson, 1918; Thiery and Brunschwig, 1955; and many others). In the present series an admixture of carcinoma and sarcoma has been seen in recurrences, involved lymph nodes and distant metastases (Fig. 25). These findings confirm that the primary growth is composite and not comparable to pseudo-sarcomatous change in the stroma of a carcinoma (Lane, 1957).

Composite sarcoma and carcinoma of the female genital tract is regarded as a form of mesodermal mixed tumour and should be so classified. It is to be distinguished from instances in which separate carcinoma and sarcoma or carcinoma and mesodermal mixed tumour coexist in the same organ (Korn, 1956). The term carcino-sarcoma of the uterus could well be discontinued.

Histogenesis

The claim that the various tumours discussed belong to the same group has so far been based on naked eye and histological features. We must now consider whether they are of similar histogenesis. Cohnheim's hypothesis that tumours

develop from superfluous embryonic rests is not now believed by most pathologists. Modification of this theory was advanced by Wilms who postulated that rests from the lumbar region are carried down with descent of the Wolffian ducts: in the female these rests may remain in the vicinity of the vestigial Gärtner's ducts. At the time of Wilms' contributions botryoid tumours of the vagina, cervix and bladder were recognized but not those of the body of the uterus. It has been pointed out that most mesodermal mixed tumours arise in sites distant from Gärtner's ducts whereas they are not found in the broad ligament (Meikle). Reputed examples of these tumours in the broad ligament have since been reported by Wurtz (1949) and Ober and Edgcombe (1954). That the displaced embryonic rests are in association with the Müllerian duct was suggested by Kehrer (1906). From his embryological studies Robert Meyer (1949) stressed the closeness of the Wolffian and Müllerian ducts during development and spoke of "illegal connexions" between them. He emphasized that mesodermal tumours of the lower genital and urinary tracts arise from sites where proximity of the two ducts is closest. Nicholson (1918, 1950) suggested that cells in the Müllerian system might respond to some stimulus with resultant tumour formation: he compared such response to that seen in certain forms of tissue metaplasia and explained the development of heterotopic tissues as a form of aberrant differentiation. MacFarland in his detailed study re-affirmed the theory of displaced embryonic rests and labelled mesodermal mixed tumours as "dysontogenetic". Willis (1948) makes the statement: "that undifferentiated rests remain in the endometrium for the whole of a woman's reproductive life, surviving multiple pregnancies and eventually producing a mixed embryonic tumour at the age of 50 or 70 is absurd." Sternberg *et al.* (1954) consider that the basic tissue of origin is endometrial stroma; they state that similar stroma is present in the endocervix of children and occasionally beneath the epithelium of the vagina in infants. These authors suggest that the origin of tumours in the vagina and cervix during childhood may thus be explained. They suggest the title "malignant mixed Müllerian tumour" for the group of neoplasms in the various age groups and sites.

Personal experience is in accord with the findings of Sternberg *et al.* (1954). It has long been generally agreed that both epithelium and stroma of the endometrium are derived from primitive Müllerian mesoderm (Figs. 26 and 27). A tumour originating from such tissue may contain a mixture of epithelial and connective tissue components. Study suggests that malignant change in the epithelium is secondary to the development of sarcoma for we find gradation from benign glands to hyperplasia and thence to carcinoma. The essential embryonic malignant growth arises from stromal cells and it is from "aberrant differentiation" of these that heterotopic structures such as cartilage and striated muscle develop. Whether it is justifiable to use the term "mixed Müllerian tumour" is doubtful. Sternberg *et al.* (1954) do not discuss botryoid tumours found in the bladder and prostate of children. These tumours, reviewed by Shackman (1950) and Hanbury (1952), usually contain heterotopic tissues and are very similar to botryoid tumours of the vagina and cervix. A survey of genital and urinary tumours has recently been carried out by White (1952).

Development of the Müllerian and Wolffian ducts has been studied by Gruenwald (1941), who states that the relationship between the ducts is so close that the conception of independent growth cannot be accepted. A corollary to this work is that of Zuckerman (1940) on the histogenesis of tissues sensitive to oestrogens; he concludes that "the embryological components of the urogenital system intermix, during development, at their points of contact". It would seem fair to conclude that mixed tumours of the female genital tract arise from Müllerian mesoderm. Tissues in close proximity to the Müllerian duct during development may give rise to similar neoplasms. Ectopic Müllerian tissue may be the site of tumour formation.

Uterine Appendages

Reports of mesodermal mixed tumours of the Fallopian tube or ovary are exceedingly rare. Scheffey, Lang and Nugent (1946) review 22 cases of sarcoma of the Fallopian tube and some of these may be mixed tumours. "Müllerian

FIG. 2

Botryoid (grape-like) tumour masses arising from the cervix of a 7-months infant. Growth also arose from the vaginal mucosa and was visible at the vulva.

FIG. 3

Polypoid growth protruding at the vulva of a 20-years old patient (see Fig. 4).

FIG. 4

Multiple grape-like masses of growth originating from the cervix of a 20-years old patient. The growth shrank considerably following deep-ray therapy so that surgical removal became possible.

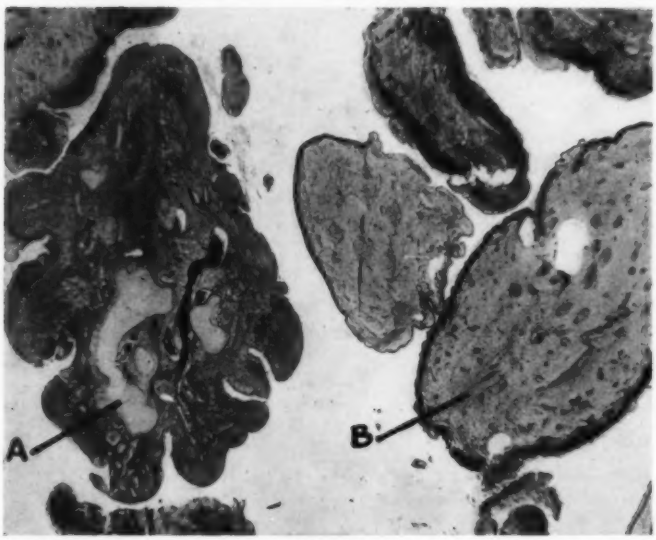


FIG. 5

Section of typical botryoid tumour of the cervix. The polypoid masses consist of myxomatous tissue in which islands of cartilage are present (A). ×10.

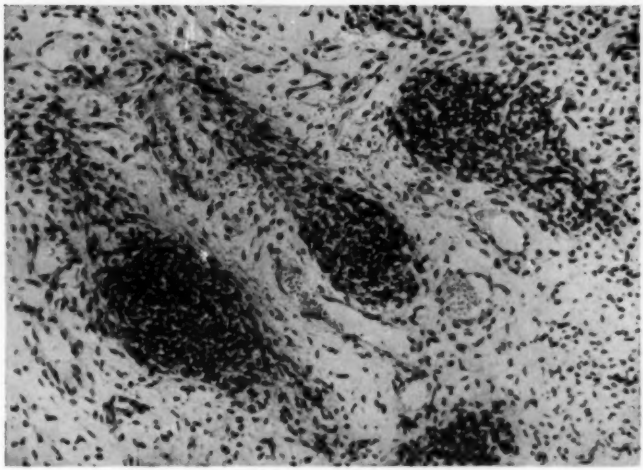


FIG. 6

Clusters of dark-staining cells in myxosarcomatous stroma—from (B) Figure 5. These aggregations are frequent in botryoid tumours and are comprised of embryonic cells. ×150.

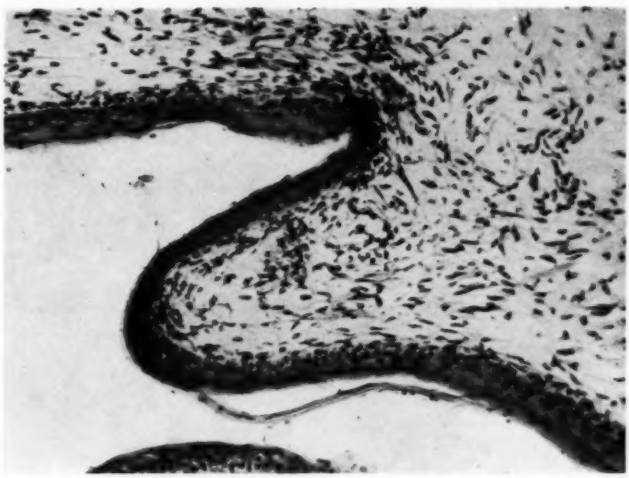


FIG. 7

Typical myxosarcomatous area covered by stratified squamous epithelium. ×200.

FIG. 8

Polypoid growth arising from the mucosa of the corpus uteri of a patient aged 15 years. Inversion of the uterus has taken place and the tumour distended the vagina.

FIG. 9

Polypoid corporeal growth in patient aged 54 years. Curettage had revealed an island of cartilage in a sarcomatous tumour.

FIG. 10

Botryoid type of growth arising in the corpus uteri of a patient aged 65 years.

FIG. 11

Polypoid corporeal tumours which distended the cavity of the uterus, dilated the cervix and projected into the vagina of patient aged 56 years. The vaginal masses are necrotic and haemorrhagic.

FIG. 12

Polypoid corporeal mesodermal mixed tumour associated with an intramural fibromyoma—patient aged 55 years. This association may lead to the wrong assumption that the growth in the cavity of the uterus is a "malignant fibroid".

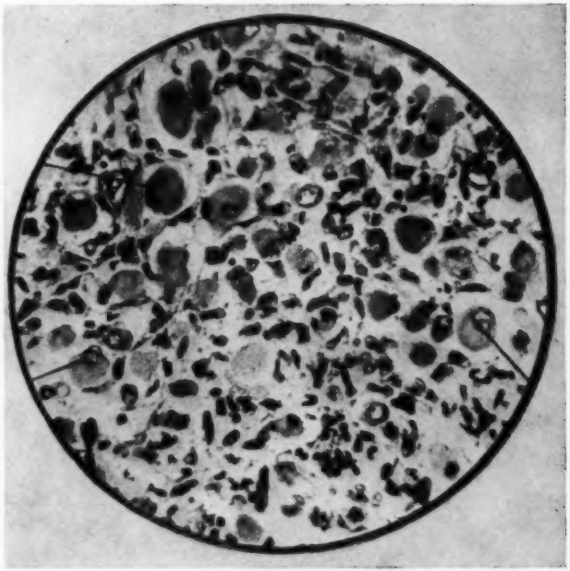


FIG. 13

Copy of illustration of "sarcoblasts" (rhabdomyoblasts) from the paper of Glynn and Blair Bell (1914).

FIG. 14

Typical rhabdomyoblasts from a corporeal tumour. The nuclei tend to be eccentric and show clumped chromatin with a darkly-staining nuclear border. The cytoplasm is acidophilic, finely granular and sometimes vacuolated. ×300.

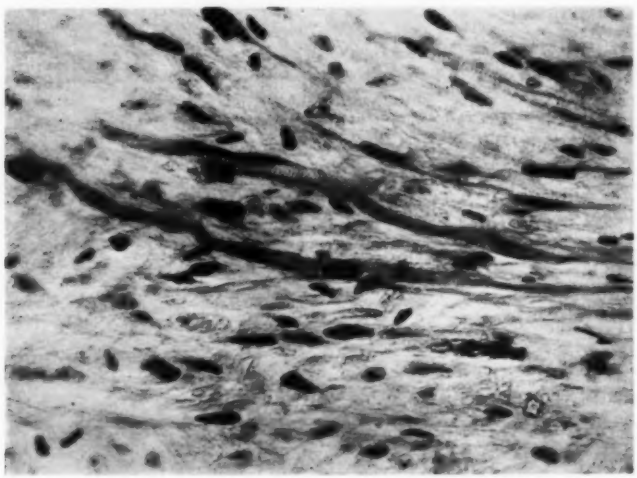


FIG. 15

Muscle fibres of varying lengths showing well-developed cross-striation. ×600.

FIG. 16

Well-developed cross-striations in a muscle fibre close to its origin. Very fine striations are present in the adjacent cell; this degree of striation is often the most that can be found in the more immature cells. ×1,000.

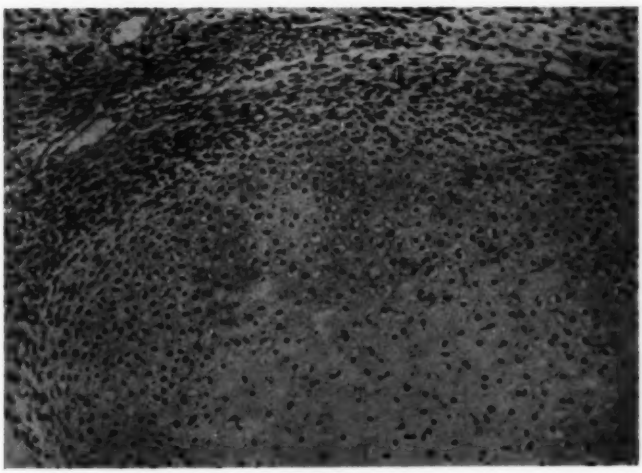


FIG. 17

Island of well-formed cartilage in a portion of cervical growth. There is surrounding sarcomatous tumour forming a pseudo-perichondrium. ×150.

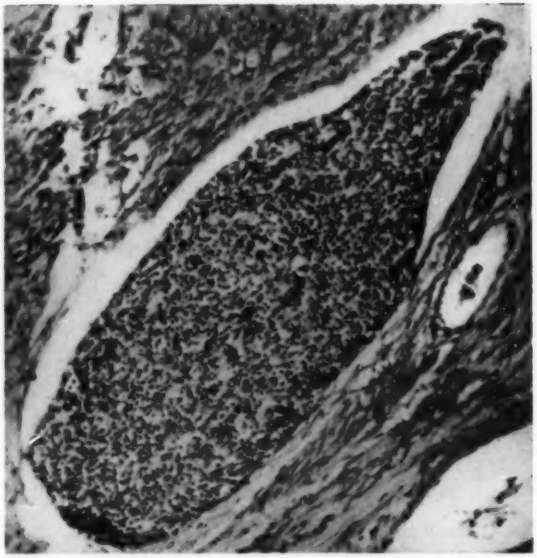


FIG. 18

Pleomorphic growth infiltrating along a lymphatic space in the myometrium. This may simulate the lesion sometimes called "malignant stromatosis". ×150.

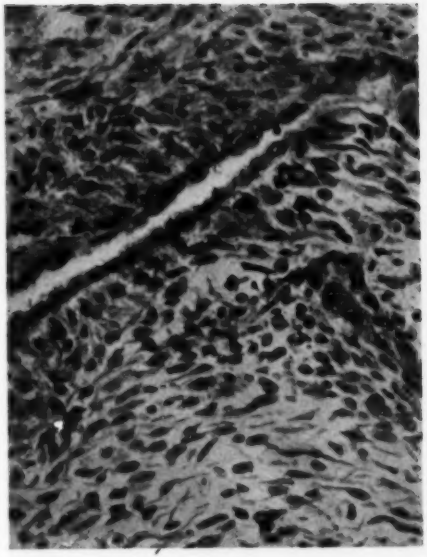


FIG. 19

Sarcomatous corporeal tumour with epithelial-lined cleft. ×225.

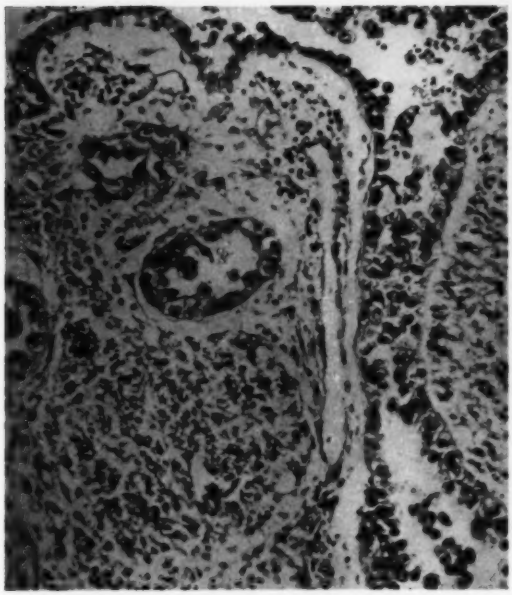


FIG. 20

A further example of a sarcomatous tumour and epithelial cleft. There are gland-like structures in the tumour substance and in this instance the epithelium is hyperplastic and suggestive of carcinoma. ×150.

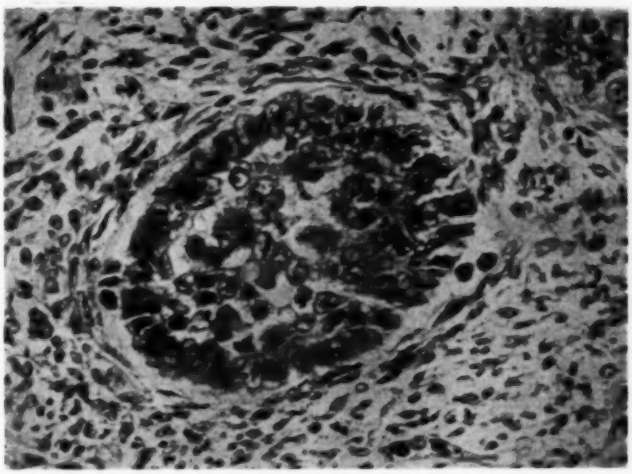


FIG. 21

An island of carcinoma in the midst of sarcoma-corporeal tumour. ×250.

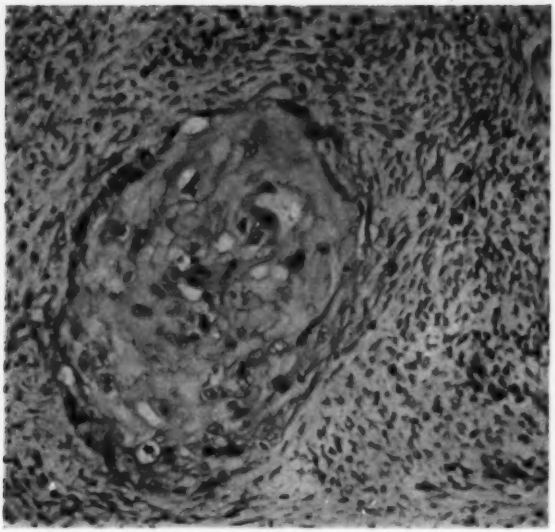


FIG. 22

An island of squamous-cell carcinoma in the midst of sarcoma–corporeal tumour. ×200.

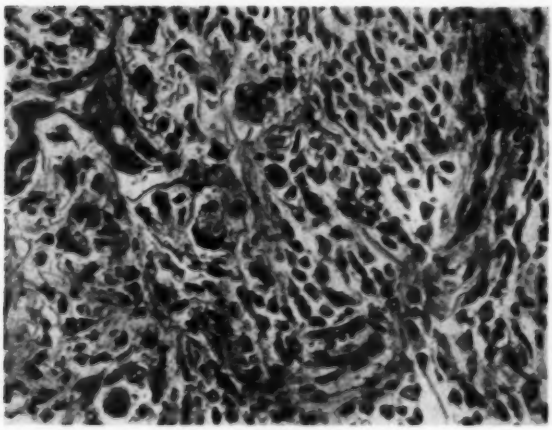


FIG. 23

An admixture of carcinoma and sarcoma: this picture is taken from the same section as that illustrated in Figure 21. ×225.

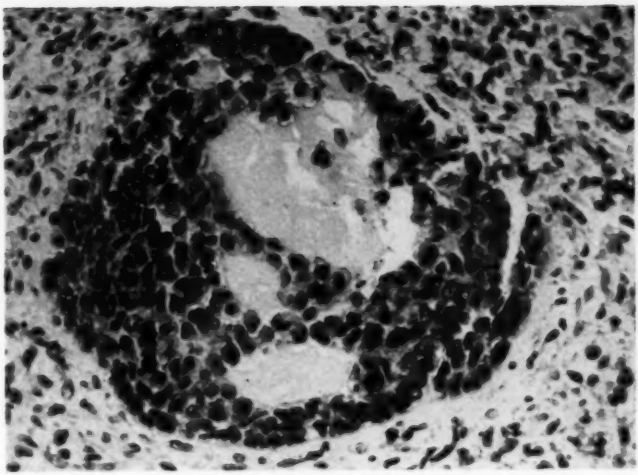


FIG. 24

An island of carcinoma resembling granulosa cell tumour due to cystic change and pseudo-rosette formation. Myxosarcoma surrounds this area. ×250.

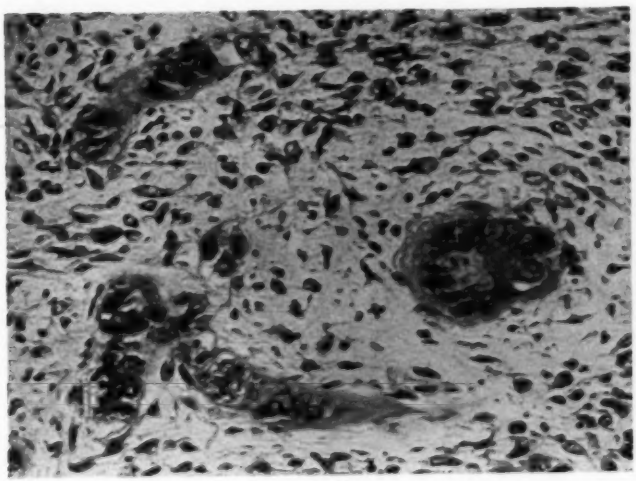


FIG. 25

A mixture of carcinoma and sarcoma from a metastasis in an abdominal lymph node—primary corporeal tumour. ×250.

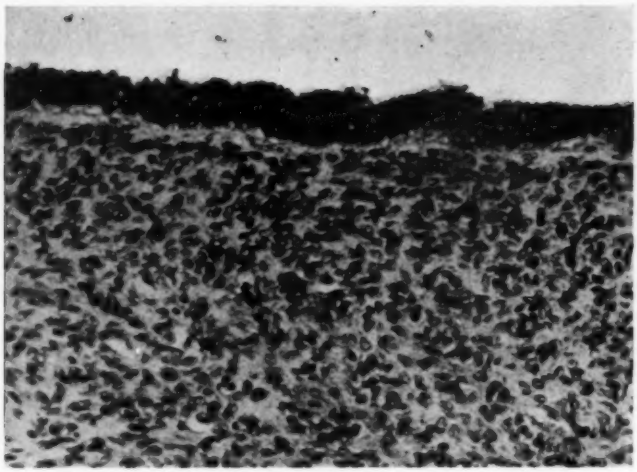


FIG. 26

Primitive Müllerian stroma and lining epithelium from the fundus of the uterus of a 20-weeks foetus. ×250.

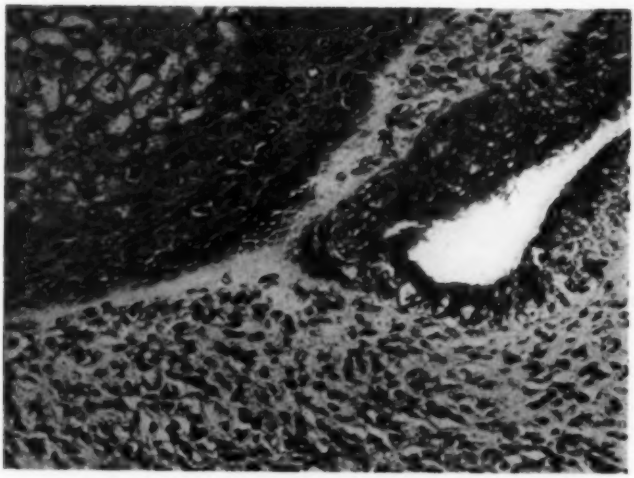


FIG. 27

Müllerian stroma from the same specimen as Figure 26 extending beneath the epithelium of the endocervix, ectocervix and vagina. ×250.

carcino-sarcoma" of the ovary is recorded by MacFarlane and Pritchard (1954): the growth is presumed to have arisen from endometriosis. An ovarian rhabdomyosarcoma is recorded by Sandison (1955); the neoplasm is comparable to mesodermal mixed tumour, containing embryonic cartilage, primitive mesenchyme and striated muscle. Teratomatous tumour development, however, is more likely in the tube and ovary than in the uterus where teratoma is exceptionally rare (Nicholson, 1956).

During the time of the present investigation 3 instances of reputed ovarian tumour having the histological features of mesodermal mixed tumour have been encountered. In none of these was the uterus removed so that the possibility of ovarian metastatic growth could not be excluded.

Aetiology

The cause of mesodermal tumours is as obscure as of other groups of neoplasms. In infants the tumour may be of embryonic type associated with developmental defect. It has been suggested (Speert and Peightal, 1949) that irradiation of the endometrium predisposes to the development of malignant disease; of 21 cases they discuss, 6 of the tumours contain sarcomatous elements. Such development of mesodermal mixed tumour is stressed by Hill and Miller (1951), who point out that the interval between irradiation and tumour formation may be 10 or more years. Klein (1953) quotes an incidence of prior irradiation in 11 of 29 examples of uterine carcino-sarcoma. On the other hand, none of the 32 patients in the combined series of Sternberg *et al.* (1954) and Thiery and Brunschwig (1955) admitted such previous therapy. In the present series of 40 cases, intra-uterine radium therapy to induce artificial menopause had been employed in 3 patients; in the remaining 37 there is no such history.

It is possible that mesodermal mixed tumours sometimes originate from uterine polyps. Fibro-adenomatous or adenomyomatous polyps may recur after curettage and develop unduly cellular stroma. Specimens of large polyps closely resembling polypoid sarcomatous tumours have been encountered. Abnormal stimulation of the endometrium by oestrogens has been suggested as a factor by Karpas and Speer—they instance the development of carcino-sarcoma in a woman who had taken oestrogens daily for 11 years following oöphorectomy. A similar case has recently been brought to the writer's attention (Crossley, 1957).

Spread

It is sometimes stated that extension of mesodermal mixed tumours is by local spread and that distant metastasis is uncommon (Amolsch, 1939; Duncan and Fahmy, 1953). In infants this may be true but perusal of published cases in older age groups shows that metastases are frequent. Following surgery, vaginal recurrence is common: local spread to the pelvic viscera with urinary obstruction often takes place. When post-mortem examinations have been performed generalized dissemination of growth has usually been found (Alznauer, 1955). Metastasis to the lungs is particularly mentioned and there are several reports of secondary deposits in the brain and in bones. Lymph nodes examined often contain deposits of growth; pelvic, para-aortic and mediastinal nodal involvement is recorded.

In the present series, based largely on study of operative material, spread of growth is gauged from case histories, follow-up records and 5 post-mortems. Vaginal and pelvic recurrence is most common but extension of growth to the abdomen is frequent. Pelvic lymph nodes were submitted for examination in only 4 instances and contained mixed tumour in 2. Distant metastases to lungs, brain, eye-lid, chest wall and lumbar muscles are noted. There are 3 patients in whom metastases developed in the spine; spread to this site is recorded by Ferreira (1951), Klein (1953), Sternberg *et al.* (1954) and others.

The histological appearances of secondary deposits are quite unpredictable: they may be the same as the primary growth, containing sarcoma, carcinoma, benign epithelial components, cartilage and striated muscle fibres. In other instances a metastasis consists entirely of sarcoma or carcinoma—examples in which some deposits show sarcoma, some carcinoma

and others a mixture with or without heterotopic components, are recorded in the abundant literature.

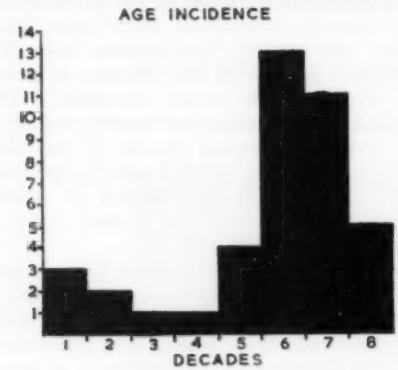
The general tendency is for metastases to be comprised of cells more anaplastic than those of the primary growth. We recall one case, however, in which striations were numerous and visible with ordinary stains in sections of a secondary tumour but found only with great difficulty in the primary growth.

Age Incidence

Mesodermal mixed tumours of the female genital tract occur at all ages (Table I). There

Table I

Number of Cases of Present Series in Each Decade



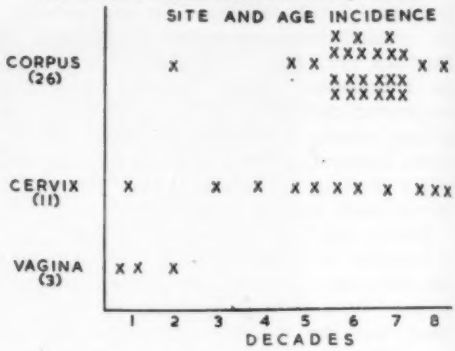
is a predilection for vaginal tumours to be found in infants and corporeal tumours in postmenopausal women but cervical growths are seen in most age groups (Table II). The relative age incidence of the occurrence of corporeal and cervical growths is comparable to the development of carcinoma in these sites (Meikle, 1936; Liebow and Tennant, 1941).

Prognosis

Reported cases show that mesodermal mixed tumours are malignant and often bring about death of the patient in a short time. The average duration of life after diagnosis is estimated at one year by Glass and Goldsmith (1941), while Hardy and Moragues (1952) suggest that in the

Table II

Cases in Each Decade Related to Site of Tumour



majority of cases death occurs within 6 months and that survival longer than 2 years is rare. There are scattered reports of longer survival (von Franque, 1893; Tracy, 1930; Randall, 1943; Ulfelder and Quan, 1947; Thornton and Carter, 1951; Webb, 1955; Thiery and Brunschwig, 1955). Important British reports include those of Hartfall (1931), who records a 5-year survival in a 66 year old patient who had a corporeal chondrosarcoma, and Dunster and Bennett (1953), who record 2 cases of botryoid sarcoma in patients aged 14 and 44 years with survival 10 and 7 years respectively after operation. Webb (1955) in a study of uterine sarcoma finds the group of mixed mesodermal tumours to yield "our best therapeutic results".

In the present series of 40 cases, 25 patients died within 4 years of treatment, 9 are alive less than 2 years after treatment but 6 have survived 4 years or longer. Some details of these 6 cases are given in Table III. From these and others reported it would seem unwise to accept the statements that radiotherapy has no place in treatment or that surgery alone is of no avail.

Association with pregnancy occurred in one case: a fleshy polyp attached by a stalk to the mucosa of the left vaginal fornix was removed by local excision from a patient 19 years of age. Three weeks later the girl was normally delivered (at 36 weeks) of a living child and is alive with no sign of recurrence a year later. Histological examination of the polyp showed a pleomorphic sarcoma with clusters of rhabdomyoblasts.

TABLE III

Patients Alive 4 Years After Therapy

Age	Tumour			Survival (years)	Therapy
	Site	Nature	Histology		
38	Cervix (Previous polyp removed)	Botryoid	Myxosarcoma cartilage striations	4½	Wertheim's hysterectomy.
48	Cervix	Botryoid	Myxosarcoma cartilage	7	Local removal. Radium. X-ray.
59	Cervix (stump)	Polypoid mass	Composite carcinoma and sarcoma	6	Radium.
54	Corpus	Polypoid mass	Composite carcinoma and sarcoma	6	Pan-hysterectomy.
59	Corpus	Polypoid mass	Composite carcinoma and sarcoma	6	Pan-hysterectomy.
65	Corpus	Botryoid	Composite carcinoma and sarcoma with cartilage	4	Pan-hysterectomy.

SUMMARY

Study of the literature and a personal series of 40 cases suggests that mesodermal mixed tumours of the female genital tract usually described under different and varied titles are a composite group of neoplasms with similar histogenesis. The tumours are not so rare as has from time to time been suggested. Recognition of further examples may help to resolve the problem of treatment.

ACKNOWLEDGMENTS

I wish to express thanks to my clinical colleagues at the Women's Hospital, Birmingham, for their co-operation and to my laboratory staff without whose help this lecture would not have been possible. I am indebted to clinicians and pathologists of other hospitals including, Messrs. Bender, Cairns, Chalmers, Cruttenden, Freeth, Galloway, Hammond, Kenny, Lawton, Maslen-Jones, Mitchell and Watson, and Doctors Cooke, Cruickshank, Dearing, Lane, Langley, McCall, McKinnell, van der Merwe, Richards, Robertson and Ward, who have allowed me to make use of specimens submitted for opinion and supplied clinical details.

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THE EFFECT OF RUPTURE OF MEMBRANES UPON LENGTH OF LABOUR

BY

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IN recent years, a growing interest has been shown in the foetal membranes and the effect they may have upon the course of labour and upon foetal welfare during the birth process. Theobald (1955) states that "a small but increasing number of obstetricians is convinced that the membranes are a liability rather than an asset during labour". Several other authors have noticed the shortening effect of early spontaneous rupture of membranes upon the first stage of labour, notably Calkins (1952) and Embrey (1953). The similar effect of amniotomy has also been mentioned but, as the patients chosen as candidates for surgical induction are usually abnormal in some way, they cannot be quoted as proof of this beneficial effect. An investigation of the whole question of the rupture of membranes therefore seemed profitable in helping to define the effect of the presence or absence of intact membranes upon the length of the first stage of labour.

SOURCES AND CRITERIA

Patients delivered consecutively in this hospital from 1953 to 1956 were investigated, multiple pregnancies and pregnancies ending in Caesarean section being excluded. There were 2,324 primiparous and 1,426 multiparous patients, a total of 3,750.

The information which forms the basis of this survey was collected from each patient's notes which had been filled in by students and midwives under the supervision of the obstetrician in charge of the case. It was checked and transferred to a punched card of the Findex system. The collection and filing of information, the counting of the cards (by a semi-mechanical method) and the analysis of the results were undertaken by one of us (M.N.B.) in order to minimize variations in the interpretation of data.

Most of the clinical factors mentioned in this paper are self-explanatory but further definition is required for the following:

(*i*) Labour is timed from the first painful contraction.

(*ii*) Occipito-posterior does not necessarily mean *persistent* occipito-posterior.

(*iii*) Postmaturity means 8 or more days after the expected date of delivery. Prematurity is determined by weight, a baby of less than 5½ pounds (2,500 grammes) being considered premature regardless of length of gestation.

(*iv*) Foetal distress is defined by a foetal heart rate of more than 160 or less than 100 per minute, or irregularity in rhythm.

(*v*) Relative disproportion is based, almost entirely, on clinical assessments.

(*vi*) "Pre-eclamptic toxaemia" is a category in which the criterion was changed during the survey; it was originally confined to patients with a diastolic blood pressure of 100 mm. Hg or more but was widened to include those who reached 95 mm. Hg at least once during pregnancy. For the purpose of this paper, no

attention has been paid to the presence or absence of albuminuria or oedema. We regret the looseness of criteria in this category but feel that these patients were sufficiently abnormal to be dealt with separately, even if their abnormality cannot with strict accuracy be called pre-eclamptic toxaemia.

Method

Primiparae and multiparae were each divided into the four groups:

(1) Those whose labours were surgically induced (referred to hereafter as A.R.M. or induction group).

(2) Those whose membranes ruptured spontaneously before the onset of labour or at the same time as the first painful contraction (S.R.B.L.). (N.B.—We have deliberately avoided using the commonly employed term "premature rupture of membranes": "premature" is unsuitable when 73 per cent of this group are at term and 18 per cent postmature and, for the vast majority of these patients, rupture of the membranes is simply the first indication of the imminent onset of labour.)

(3) Those whose membranes ruptured during the first stage of labour (called "1st stage rupture group").

(4) Those whose membranes ruptured at full dilatation or during the second stage of labour (called "2nd stage rupture group").

In groups (3) and (4) no distinction was made between spontaneous and artificial rupture.

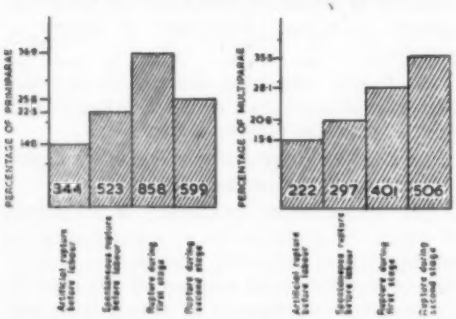

Fig. 1

Percentage of patients in each rupture group.

Figure 1 shows the percentage of patients in each of these groups.

For each of the four groups the following factors were tabulated:

(1) Length of first stage.

(2) Length of second stage.

(3) Age of mother.

(4) Weight of baby.

(5) Maturity.

(6) Post-partum haemorrhage.

(7) The incidence of forceps delivery, manual removal of placenta, relative disproportion, abnormal presentations (breech and occipito-posterior only), foetal distress, stillbirths and "pre-eclamptic toxaemia". No other maternal diseases were investigated as the numbers of each were too small.

The incidence of these factors for primiparae and multiparae is shown, as a percentage, in Tables I and II respectively. In column (a) is the average percentage incidence of each factor in all primiparae or multiparae; in columns (b), (c), (d) and (e) is the incidence of each factor in each of the four "rupture groups" described. The figures in these columns were compared with those in column (a) and an attempt made to illustrate the statistical significance of the differences diagrammatically in the remaining four columns. (See key attached to figures.)

Effect of Membranes Upon the Length of Labour

We have used the percentages in Tables I and II to construct Figure 2, illustrating the average length of the first stage of labour for each of the four groups.

It can be seen that the four curves in each diagram form pairs, and that there is a similarity between the curves for the two groups in which membranes are already ruptured by the time labour starts, and also between those for the two groups in which they remain intact for at least part of labour; the first pair have shorter labours than the second pair; the difference in length being statistically very significant.

TABLE I

Primiparae

	(a) All Patients	(b) Artificial Rupture	(c) Spontaneous Rupture Before Labour	(d) First Stage Rupture	(e) Second Stage Rupture	Artificial Rupture	Spontaneous Rupture Before Labour	First Stage Rupture	Second Stage Rupture
1st Stage:	Per cent	Per cent	Per cent	Per cent	Per cent				
Over 80 hours ..	0·26	0	0·2	0·5	0·2	×	×	×	×
80— hours ..	6·45	4·6	5·15	9·2	4·5	□	□	+	−
40— hours ..	19·14	12·8	14·3	23·0	21·5	−	−	+	□
20— hours ..	34·44	30·2	29·1	36·3	39·6	□	−	□	+
10— hours ..	26·62	30·7	33·6	21·6	25·2	□	⫲	−	□
5— hours ..	12·81	21·5	17·0	9·3	9·0	+	⫲	÷	−
2nd Stage:									
2+ hours ..	7·31	8·4	7·8	7·5	6·0	□	□	□	□
Under 2 hours ..	40·68	41·8	39·3	42·6	38·2	□	□	□	□
¾— hours ..	45·37	42·3	44·5	45·6	47·4	□	□	□	□
¼— hours ..	6·58	7·3	7·8	4·3	8·4	□	□	−	+
Age:									
40+	0·34	0·6	0·8	0·1	0·2	×	×	×	×
40—	3·14	4·6	2·7	3·3	2·5	□	□	□	□
35—	11·83	11·3	12·8	12·3	10·5	□	□	□	□
30—	32·98	32·8	32·0	34·7	31·6	□	□	□	□
25—	42·36	42·9	41·7	41·1	44·4	□	□	□	□
20—	9·29	7·5	10·1	8·4	10·9	□	□	□	□
Baby's Weight:									
Over 8 pounds ..	22·57	23·2	17·3	25·4	22·7	□	−	+	□
6–8 pounds ..	68·20	65·5	70·5	68·7	66·6	□	□	□	□
Under 6 pounds ..	9·16	11·0	11·6	5·8	10·7	□	+	÷	□
Post-mature	21·46	39·2	12·5	20·7	20·0		÷	□	□
Term	74·56	55·1	81·7	77·3	75·2	÷	⫲	+	□
Premature	3·91	5·5	5·1	1·9	4·8	□	□	÷	□
Post-partum Haemorrhage:									
20+ ounces ..	2·32	1·7	2·1	2·1	2·8	□	□	□	□
19— ounces ..	13·16	14·8	14·1	13·3	11·0	□	□	□	□
10— ounces ..	84·45	83·5	83·8	84·6	86·2	□	□	□	□
Forceps delivery	9·16	10·4	10·8	9·6	6·4	□	□	□	−
Manual removal of placenta ..	3·23	3·2	3·2	3·7	2·5	□	□	□	□
Relative disproportion ..	2·75	3·5	2·3	3·7	1·3	□	□	+	−
Breech	1·98	0·6	1·9	2·4	2·2	□	□	□	□
Occipito-posterior	2·58	2·6	2·7	2·4	2·7	□	□	□	□
Foetal distress	8·34	10·4	6·3	9·9	6·7	□	−	+	□
Stillbirths	1·42	1·7	1·1	1·2	1·8	×	□	□	□
"Pre-eclamptic toxaemia" ..	10·06	40·0	7·3	4·5	3·2	+	−	÷	÷

KEY

□ very near average or not *significantly* different. + significantly greater than average incidence: standard deviation×2. ⫲ significantly greater than average incidence: standard deviation×4 or more. − significantly less than average incidence: standard deviation×2. ÷ significantly less than average incidence: standard deviation×4 or more. × too few cases.

Multiple pregnancies and deliveries by Caesarean section are excluded.

TABLE II

Multiparae

	(a) All Patients	(b) Artificial Rupture	(c) Spontaneous Rupture Before Labour	(d) First Stage Rupture	(e) Second Stage Rupture	Artificial Rupture	Spontaneous Rupture Before Labour	First Stage Rupture	Second Stage Rupture
1st Stage:	Per cent	Per cent	Per cent	Per cent	Per cent				
Over 80 hours ..	0·21	0	0	0·5	0·2	×	×	×	×
80— hours ..	1·8	1·4	1·6	2·4	1·8	□	□	□	□
40— hours ..	9·10	4·5	6·1	12·9	9·9	□	□	□	□
20— hours ..	24·89	19·8	18·2	28·9	27·8	□	−	+	+
10— hours ..	30·07	31·5	26·3	31·6	30·3	□	□	□	□
5— hours ..	33·79	42·8	47·9	23·4	29·7	+	⫞	÷	−
2nd Stage:									
2+ hours ..	0·77	0·5	0	1·7	0·6	×	×	×	×
Under 2 hours ..	8·20	8·1	9·8	7·7	7·7	□	□	□	□
½— hours ..	45·99	46·8	50·9	45·6	43·3	□	□	□	□
¼— hours ..	45·0	44·6	40·1	44·8	48·1	□	□	□	□
Age:									
40+	4·63	5·9	6·1	3·5	4·1	□	□	□	□
40—	11·64	17·1	15·2	10·2	8·3	+	□	□	−
35—	27·76	25·7	29·0	28·4	27·4	□	□	□	□
30—	32·39	35·1	30·0	31·6	33·1	□	□	□	□
25—	21·66	15·8	17·9	24·2	24·4	□	□	□	□
20—	1·89	0·5	2·0	2·0	2·4	×	□	□	□
Baby's Weight:									
Over 8 pounds ..	34·07	33·4	29·6	39·1	32·9	□	□	+	□
6–8 pounds ..	56·36	56·3	54·9	55·0	58·1	□	□	□	□
Under 6 pounds ..	9·53	10·4	15·5	5·7	8·7	□	+	−	□
Postmature	20·96	36·0	17·5	18·9	17·9	⫞	□	□	−
Term	74·52	59·9	73·1	79·4	77·6	÷	□	+	+
Premature	4·49	4·1	9·4	1·5	4·1	□	+	−	□
Post-partum Haemorrhage:									
20+ ounces ..	3·43	3·2	3·4	2·9	3·9	□	□	□	□
19— ounces ..	12·27	14·4	11·8	11·7	12·0	□	□	□	□
10— ounces ..	84·26	82·4	84·8	85·4	84·1	□	□	□	□
Forceps delivery	2·59	2·3	3·4	2·5	2·4	□	□	□	□
Manual removal of placenta ..	2·24	2·3	2·0	3·5	1·4	×	□	□	□
Relative disproportion ..	1·05	0·9	0·3	2·4	0·6	×	×	×	×
Breech	2·03	2·7	4·0	1·9	0·6	×	+	□	−
Occipito-posterior	3·08	3·6	3·7	1·5	3·7	□	□	−	□
Foetal distress	4·69	7·7	5·7	3·2	3·9	+	□	□	□
Stillbirths	1·61	1·4	1·7	1·7	1·6	×	×	□	□
"Pre-eclamptic toxaemia" ..	9·04	36·5	4·0	4·2	3·8	⫞	−	÷	÷

KEY

□ very near average or not *significantly* different. + significantly greater than average incidence: standard deviation×2. ⫞ significantly greater than average incidence: standard deviation×4 or more. − significantly less than average incidence: standard deviation×2. ÷ significantly less than average incidence: standard deviation×4 or more. × too few cases.

Multiple pregnancies and deliveries by Caesarean section are excluded.

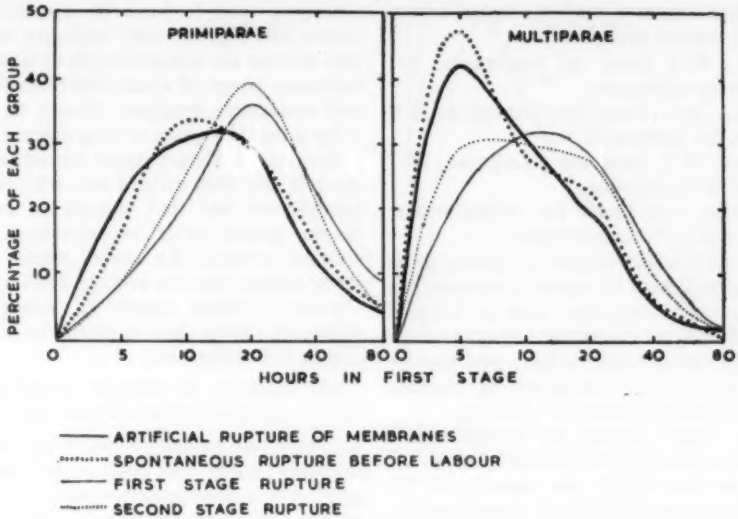

FIG. 2

Average length of first stage in each rupture group.

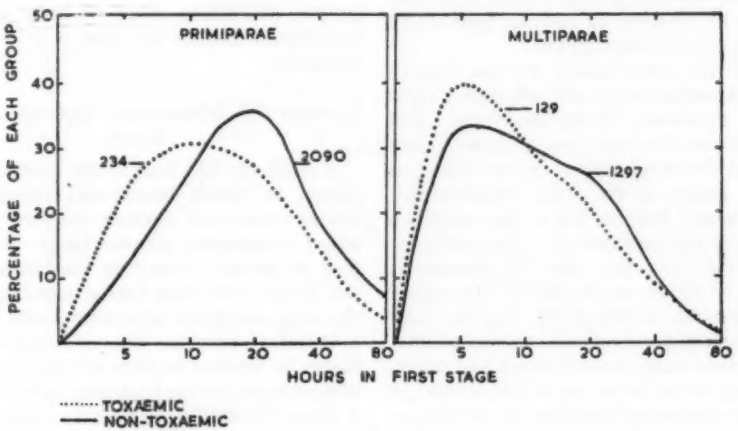

FIG. 3

The shortening effect of pre-eclamptic toxaemia upon the first stage of labour.

N.B. The figures by the graphs are the number of patients for each survey.

The average lengths of the first stage of labour for the four rupture groups are:

(1) A.R.M., 13·5 hours for primiparae, 8·3 hours for multiparae.
(2) S.R.B.L., 14·2 hours for primiparae, 9·9 hours for multiparae.
(3) 1st stage, 19·2 hours for primiparae, 12·7 hours for multiparae.
(4) 2nd stage, 16·6 hours for primigravidae, 11·0 hours for multigravidae.

Thus it would seem desirable for labour to be preceded by rupture of the membranes since this results in a shorter first stage, and, as Tables I and II show, has no significant effect upon the length of the second stage or upon post-partum haemorrhage or the incidence of forceps deliveries or manual removal of placenta.

However, other factors are present which might influence the length of labour, such as the mother's age, the weight and maturity of the child and the presence of relative disproportion, abnormal presentations and pre-eclampsia. If these are distributed equally throughout the four groups they may be ignored, but if they are not they must be examined separately, in order to make sure of the importance of the part played by the membranes.

The mother's age is not distributed very differently in the four groups. There is a small increase in the number of patients aged 36–40 occurring in the induction group.

Some of the other factors are too rare to influence the general trend, even where they show significant deviations from the mean. For example, relative disproportion increases significantly in the first stage rupture group, that is, as one would expect, in the group which experiences the longest labours, but as this condition occurs in only 64 primiparae (2·75 per cent) and 15 multiparae (1·05 per cent) its presence is unlikely to be wholly responsible for the greater length of labours in this group. For the same reason, abnormal presentations can be neglected.

On the other hand, pre-eclampsia and weight and maturity of the baby are factors which are distributed very unequally and which are thought by some writers to affect length of labour; they must therefore be dealt with at greater length.

(a) *Pre-eclampsia.* Clinical impression, borne out by our figures, is that patients with pre-eclampsia tend to have shorter labours than others (see Fig. 3); their inclusion must therefore shorten the average length of labour for the induction group, of which they form 40 per cent, and conversely lengthen labours in the three other groups by virtue of their absence.

However, if these patients are separated from the rest and then divided into the four rupture groups, we find that rupture of membranes before labour onset is associated with the shortest labours, the actual length of labour being shorter than the average in all four groups —about 2 hours shorter in primiparae, the difference being less marked in multiparae. Figure 4 illustrates this.

(b) *Maturity.* In contrast, postmaturity has been claimed to lengthen labour (see Fig. 5).

Postmature patients form 39 per cent of the induction group and, while it may be noted in passing that their presence balances the 40 per cent pre-eclamptic patients, it is seen in Figure 6 that, no matter what the maturity may be, the rupture of membranes before labour onset is again associated with shorter labours. (Premature babies are omitted here as they are included in the "under 6 pounds" group in the following section.)

(c) *Weight of Baby.* Figure 7 shows that the general shortening effect of early rupture of membranes remains the same as in the previous categories.

Rupture of Membranes During the First Stage

A similarity has been noted between the two groups in which membranes rupture before labour onset, and between the two groups in which membranes remain intact for at least part of labour. It may be questioned whether the division into these four groups is a real one; that is to say, while there is no doubt in Groups 1, 2 and 4 about the time of rupture of membranes in relation to stage of labour, it is often difficult to define the beginning of the first stage; if there is indeed no clear-cut division between Groups 2 and 3, that is, if most membranes rupture shortly after the first painful contraction, then the contrast which we have found between them would be invalid.

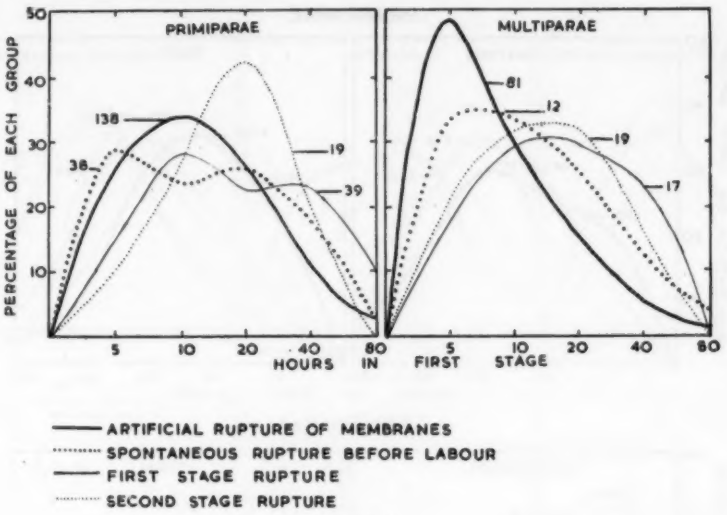

FIG. 4

Pre-eclamptic patients: length of first stage in each rupture group.

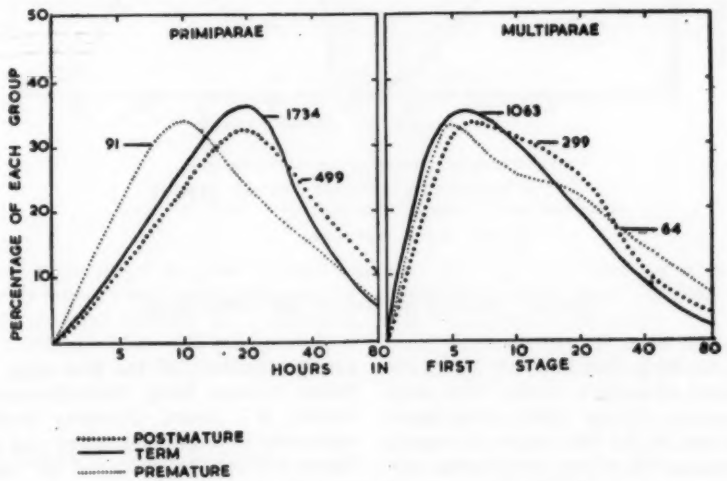

FIG. 5

The lengthening effect of postmaturity upon the first stage of labour.

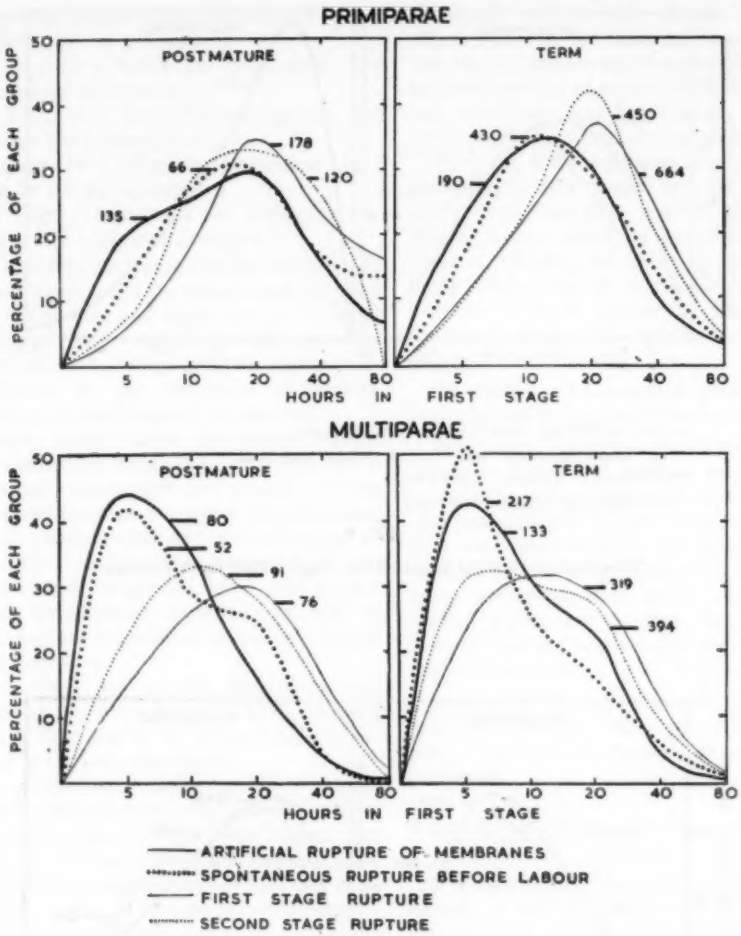

FIG. 6

Maturity: length of first stage in each rupture group.

However, we do in fact find that by far the greater number of patients in the "first stage rupture" group rupture their membranes towards the end of the first stage: in a group of 256 primigravidae whose membranes ruptured during the course of the first stage we found that 66·4 per cent of the ruptures occurred during the last quarter of the first stage, the average duration of the first stage of labour before rupture being 14·1 hours and after rupture 4·7 hours. Grouping these patients separately is therefore justified and the resemblance between this group and the "second stage rupture" group is explained.

In support of this, Calkins (1952) has also noted that rupture of the membranes soon after

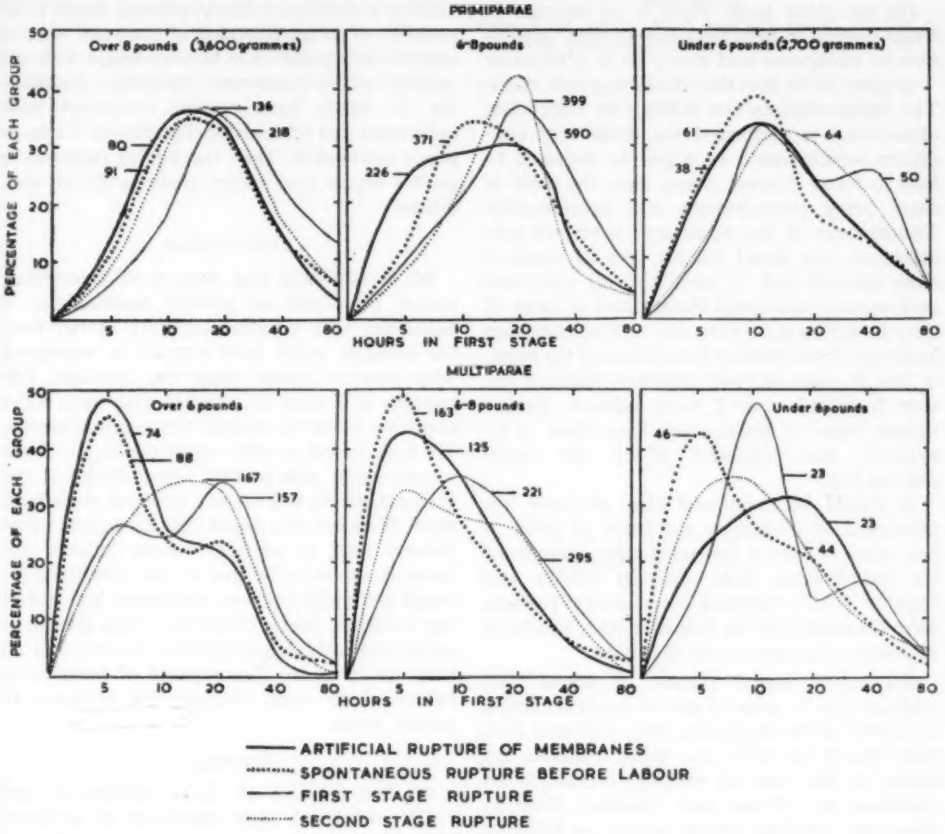

FIG. 7

Weight of baby: length of first stage in each rupture group.

labour onset gives almost as good a result as rupture before labour onset and he suggests that any attempt to give impetus to a desultory labour by artificial rupture will only succeed if it is done very early—in fact, before the need for it becomes apparent.

DANGERS OF EARLY RUPTURE

We have tried to ascertain whether rupture of membranes before labour onset brings any undesirable consequences which might outweigh the advantages of shortening labour. The two investigated were foetal distress and genital sepsis following amniotomy.

(a) *Foetal Distress.* It seems probable that, in primiparae at least, foetal distress may be related to length of labour since there is a marked increase in the "first stage rupture group" (the longest labours) and a marked decrease in the "spontaneous rupture before labour group" (the shortest natural labours). The same relationship is not shown in multiparae because labours are shorter in every group.

On the other hand, there is an increase in foetal distress in both induction groups—significant in multiparae and nearly so in primiparae—in spite of the fact that the labours are short. The explanation is not difficult to find, since amniotomy is performed for those very conditions which would or might be expected to lead to foetal distress in any case, the chief of these being pre-eclampsia and postmaturity. Twenty-three of our primiparae combined pre-eclampsia and foetal distress, and of these 11 were induced and 12 were not; 49 combined postmaturity and foetal distress and of these 18 were induced and 31 were not. A third condition leading to foetal distress is smallness of the baby: of the 26 cases of foetal distress weighing less than 6 pounds only 2 were induced. Similar figures occur in multiparae. Thus there is no evidence that induction affects the foetal distress rate.

It should be mentioned that we have not attempted to investigate the effect of delay in the onset of labour following early rupture of the membranes. Both Embrey (1953) and Calkins (1952) studying spontaneous rupture, have observed that the risk to mother and baby increases in proportion to the delay.

(b) *Genital Sepsis* (Sepsis of uterus and vagina). The 77 cases of genital sepsis occurring in vaginal deliveries during 1953, 1955 and 1956 (the figures for 1954 not being available for study at the time of writing) represents an incidence of 1·9 per cent. Dividing these 77 cases into our four rupture groups we find that 25 per cent of the sepsis cases occurred in the induction group which represents 15 per cent of all patients, 18 per cent occurred in the "spontaneous rupture before labour group" which represents 22 per cent of all patients, 30 per cent occurred in the "first stage rupture group" which represents 34 per cent of all patients and 27 per cent occurred in the "second stage rupture group" which represents 29 per cent of all patients.

These figures show an apparent rise in the occurrence of sepsis in conjunction with amniotomy and a fall in the other three groups; in no case is this statistically significant, whereas examination of the case notes for each patient shows that it might be attributed with equal validity to forceps delivery, manual removal of placenta or to the retention of products of conception. It should also be mentioned that all patients whose membranes have been ruptured for 24 hours have routine treatment with antibiotics and often oxytocin infusion if labour is not established. Thus the figures represent a genital sepsis rate under these artificial conditions.

Conclusions

We have found that rupture of membranes before the onset of painful contractions is associated with labours which are shorter than the average, while later rupture is associated with labours longer than the average; this remains true even of patients who have some condition likely to influence the length of labour. We have found no effect upon the length of the second stage, post-partum haemorrhage or the forceps delivery and manual removal of placenta rates. We have also found that the higher foetal distress rate in patients whose labours are induced seems to be due to the condition for which the induction was performed and not to the induction itself; otherwise foetal distress is associated with longer labours. We can find no evidence to prove that rupture of membranes before labour onset increases the incidence of genital sepsis.

Summary

(1) The labours of 2,324 primiparae and 1,426 multiparae were examined to ascertain the effect of intact and ruptured membranes upon the length of labour.

(2) It was shown that labours longer than average are associated with intact membranes, and shorter than average with ruptured membranes.

(3) The possible adverse effect of ruptured membranes on the foetal distress and genital sepsis rates was investigated but no positive contra-indication to rupture was found.

Acknowledgments

This survey is part of the larger programme of obstetric research made possible by the generosity of the Nuffield Foundation.

We should like to express our thanks to the staff of University College Hospital for their co-operation and advice, and more particularly to Miss A. Hart for her invaluable clerical assistance.

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EXTERNAL TOCOGRAPHY IN THE STUDY OF UTERINE MOTILITY

A Critical Examination of the Method

BY

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IN an earlier communication (Embrey, 1955a) details were published of a new multichannel "Hydroflex" external tocograph, employing a simple form of hydraulic recording suitable for routine use. More recently the value of the instrument has been established in several studies of the effect of drugs on uterine activity (Embrey and Garrett, 1955; Garrett and Embrey, 1955). A now fairly extensive use of the tocograph has confirmed its utility and shown that it provides a ready and useful means of recording uterine activity in pregnancy, labour and the puerperium. Its usefulness in clinical practice has been repeatedly proved in the control of oxytocin infusions.

Despite these favourable impressions, increasing experience has demonstrated the limitations of external tocography—limitations which it would seem are not always appreciated. An external tocograph will record accurately the frequency and duration of the contractions, will give a measure—though not of course in absolute units—of their amplitude, and will provide a valuable overall record of uterine action.

But, as already pointed out (Embrey, 1955b) in studying the results of external tocography, especially multichannel recording, there would seem to be a real danger of misinterpretation—or, at least, of attaching elaborate interpretations to phenomena which permit of simple explanation. It may be a reflection of this danger that, despite a vast amount of tocographic experiment in recent times, our understanding of uterine contractility remains incomplete and confused by disharmonious hypothesis. Thus, while Murphy (1947) makes much of the ability to measure uterine tone with an external tocograph and consequently claims to distinguish hypertonic and hypotonic uterine activity, Reynolds and his colleagues (1948a, b, 1954) make no claim to do so, but instead lay emphasis on the importance of fundal dominance and the gradient of uterine activity.

As will be shown, the method is beset with pitfalls, and its limitations are such as to leave reason to doubt whether external tocography by itself can provide a satisfactory means of measuring uterine tone or, for that matter, of demonstrating any segmental differences of uterine contractility.

FALLACIES IN EXTERNAL TOCOGRAPHY

The Influence of the Parieties

Uterine Tone. The attempted measurement of uterine tone by an external tocograph depends on the supposition that tone will be proportional to displacement of the receptor head when the instrument is applied to the abdomen with constant force.* On this view the resting tone of

* In the case of the Hydroflex tocograph, the instrument can be fitted in place of the usual base ring with a circular base plate 3 inches in diameter through which the receptor head of the Hydroflex bellows just projects. The recorder is then applied to the abdomen with sufficient force to flatten the area of skin in contact with it, and the pen deflection noted. In multichannel recording there is a simple provision to ensure that each recorder is applied to the abdomen with the same force. The exact pressure of application is not as critical as might be imagined. With successive increments of pressure, the registered deflection increases progressively until the area of contact is flattened, then reaches a plateau when it is remarkably unaffected by pressure changes. Thereafter, it is only influenced again when force is excessive.

Very recently Smyth (1957) has described a single channel strain gauge external tocograph (called the guard ring tocodynamometer) in which the same principle is employed. He maintains that, providing the receptor head and the circular base plate are in the same plane and the instrument is applied to the abdomen with sufficient force to flatten the corresponding area of the uterus, it will accurately record intra-uterine pressure.

the uterus is represented in the record by the base line between contractions. This might be well enough if the instrument could be applied directly to the uterus, but the interposition of the abdominal parieties and extra-uterine soft tissues must be remembered—while, as will be shown later, the uterine contents cannot be disregarded. Hence, the most that can be expected of an external tocograph is an estimate of the composite "tone" of all the underlying tissues.

Experience indicates that estimations of uterine tone with an external tocograph are so influenced by extraneous factors as to make them fallacious. A gradual lowering of the base line or "tone" soon after the commencement of recording is a quite common phenomenon in external tocography which has been observed by Wolf and recently commented on by Huber (1956); it probably represents the influence of the parieties rather than a true lowering of uterine tone.

The manner in which estimations of "tone" are influenced by the extra-uterine tissues has been demonstrated several times. When the opportunity has presented of examining a patient during labour with a distended (abdominal) bladder, estimations of "tone" of the lower uterine zone have been made before and after relief of the retention. Figure 1

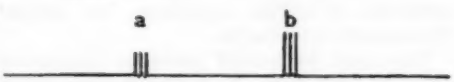

FIG. 1

Estimations of "tone" of lower uterine zone, (*a*) with full bladder, (*b*) after emptying bladder.

illustrates the result in a particular case and clearly shows that "tone" estimations are in fact influenced by changes in the extra-uterine tissues.

Multichannel Pattern of Uterine Contractility. The pattern of "fundal dominance" with a "gradient of activity" from fundus to lower segment, claimed by Reynolds *et al.* (1948a, b, 1954) to be characteristic of normal uterine action, has seldom been demonstrated with the multichannel Hydroflex external tocograph. Rather it has been found with the recorders placed in the upper, middle and lower uterine zones—centrally in squares 2, 5 and 8 which, be it noted, do not necessarily correspond with the upper, middle and lower segments—the greatest activity has almost always been recorded in the middle zone (Fig. 2a). Thus, in a controlled

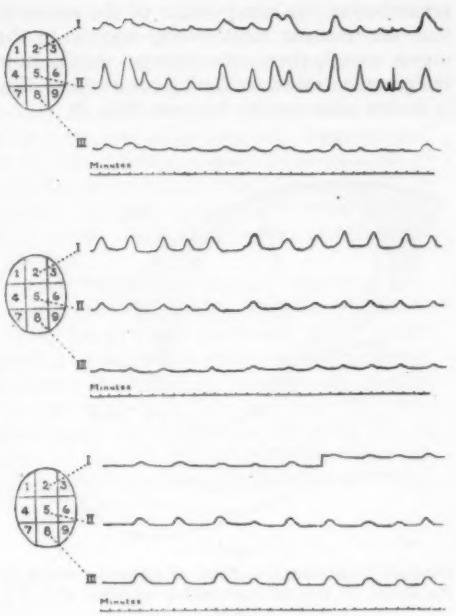

FIG. 2

Three-channel external tocographic records showing (*a*) mid-zone dominance, (*b*) upper zone dominance, (*c*) lower zone dominance.

Note: Increased "tone" in upper channel due to change of foetal position.

series in 20 consecutive cases in pregnancy, the greatest activity was in the mid-zone in 17 and in the lower zone in 3; while in 20 consecutive cases in labour, mid-zone dominance was present in all.

Now this mid-zone dominance has been observed by others (Huber, 1956), and is what might be expected. The physical basis of external tocography, it must be admitted, is still a matter

for conjecture.* However, during uterine contraction there is undoubtedly (*a*) palpable hardening of the uterus and, according to most authorities, (*b*) anterior displacement of the uterus as it rotates around its cervical attachments and becomes more erect. It is probable that both are appreciated to a greater or lesser degree. If this be so, it would seem reasonable, remembering the interposition of the parieties, that the recorder most closely applied to the uterus, namely the middle recorder, should show the greatest movement during contraction. This is in fact what usually happens (Fig. 3).

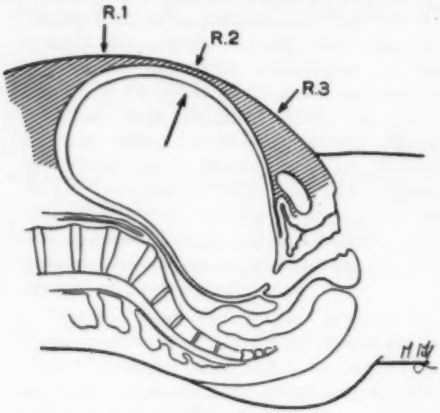

FIG. 3
Diagram illustrating the effects of forward rotation of the uterus on external tocographic recorders (R1, R2, R3).

There are, however, a few exceptions to the general rule. Occasionally, with the receptors situated caudally in squares 2, 5 and 8, a downward gradient of activity with fundal dominance has been produced (Fig. 2b). But more frequently a reversed gradient of activity and lower zone dominance has been observed (Fig. 2c).

A good deal depends on the actual positions of the recorders. Figures 4a and b show how by moving the recorders caudally, but still confining them to squares 2, 5 and 8, a normal

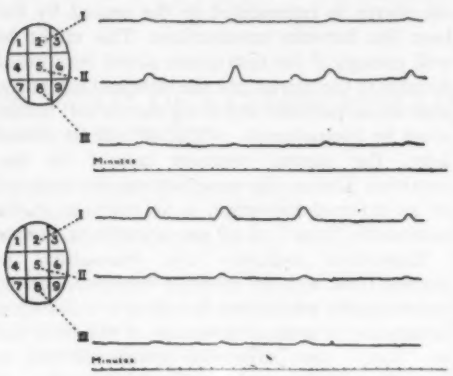

FIG. 4
Three-channel external tocographic records showing (*a*) mid-zone dominance, (*b*) upper zone dominance artificially produced by moving recorders caudally.

picture of mid-zone dominance can sometimes be converted into one of fundal dominance with a gradient of activity. On the other hand this has not often been possible and frequently the recorders have been moved correspondingly without effect on the pattern of mid-zone dominance.

Now, some observers have been tempted to attribute such variations of pattern to disturbances of uterine physiology, but simpler explanations are possible.

The usual pattern of mid-zone dominance obtained with the Hydroflex tocograph is merely indicative of the influence of the parieties on the recordings, and the occasional variations observed can be frequently explained as an effect of extra-uterine factors. The influence of the extra-uterine soft tissues is also seen in another way. In Figure 6a it will be noticed that the relative dominance of the lower channel actually increased as recording proceeded over the course of half-an-hour. One need not seek any elaborate or subtle explanation of this observation. The bladder, having been emptied at the start, was found to contain 10 ounces of urine after recording; and it would seem probable that elevation of the foetal head due to bladder distension caused the accentuation of lower zone preponderance.

* Many explanations have been forthcoming. Reynolds for example maintains that his tocodynamometer records uterine contractions by virtue of a decrease in the radius of the uterus. Halliday and Heyns (1952) however question this view on theoretical grounds.

The Influence of the Foetus

Uterine Tone. The influence of the foetus on external tocographic recordings is not sufficiently appreciated. If only the uterus and abdominal parieties had to be considered in estimation of uterine tone then it might be expected (bearing in mind the thickness of the elastic parieties) that tone would be highest near the centre of the abdomen; but repeated experiment shows that the most important influencing factor in this matter is the foetal position, and that "tone" is always exaggerated over a foetal part.

The influence of foetal parts has many times been seen (Fig. 2c) and has on several occasions been graphically demonstrated by the following simple experiment. Applying the tocograph each time with a constant force, records of resting "tone" have been obtained from points scattered over the pregnant uterus. The observation, in arbitrary units (the inverse of the mathematical square was the unit adopted), has then been represented on a plan of the abdomen, each area with its appropriate proportional intensity of hatching. Figure 5 indicates the result and illustrates not only that "tone" is high over a foetal part, but that if a sufficient number of observations are taken a tolerable representation of the foetus will result. The accuracy of this "palpation by tocography" naturally varies with the thickness of the abdominal wall and the amount of liquor, evidence of the effect of the latter being provided by the relatively uniform records of "tone" obtained in a case of hydramnios.

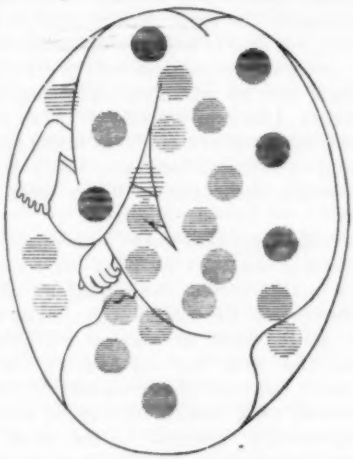

FIG. 5

Estimations of "tone" diagrammatically represented by hatching of appropriate density to indicate the influence of foetal parts.

Multichannel Pattern of Uterine Contractility. Just as the level of "tone" is influenced both by the abdominal parieties and the uterine contents, so too is the amplitude of contractions, and hence the multichannel patterns of uterine contractility. The effect of these extraneous factors can be quite frequently observed. For example, it is probably significant that the dominance of the lower zone seen in Figure 2c was recorded in a patient who had a posterior placenta praevia which caused noticeable forward displacement of the head.

In any event, three-channel recording in a patient with a "high head" during late pregnancy or early labour quite frequently shows lower-zone dominance, which might be interpreted by the unwary as indicating an abnormal gradient of activity (Fig. 6a). That the lower zone preponderance is due to the presence of the head is proved by the fact that it disappears when the head sinks into the pelvis either before or during labour (Fig. 6b).

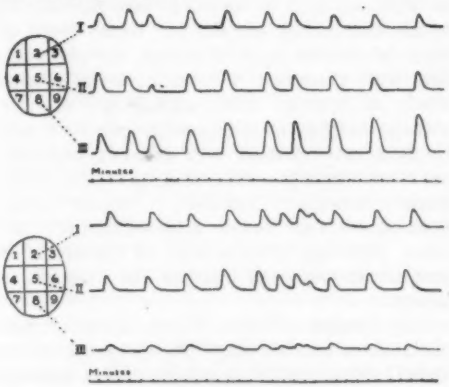

FIG. 6.

Three-channel external tocographic records showing (*a*) lower zone dominance associated with a high head. *Note:* Increasing preponderance of lower channel. (*b*) Mid-zone dominance recorded in same patient after descent of head.

Correlation of Uterine Motility and Progress in Labour

Delay in labour—in the absence of disproportion or malpresentation—is usually attributed to faults in the expulsive forces. On this view it is believed that when the contractions are weak and infrequent, or irregular and incoordinated, labour is prolonged. On the other hand, it is assumed—and Murphy (1947), Reynolds (1951), Alvarez and Caldeyro-Barcia (1953), Reynolds *et al.* (1954), and others have claimed—that in normal labour the contractions are regular in intensity and frequency and that the stronger the contractions the more rapid the progress of labour.

Attempts in the present study to correlate the degree of uterine activity, as revealed by external tocography, with the clinical phenomena of labour have not proved very fruitful. One of the difficulties, of course, is that of estimating the work done by the uterus, for while the duration and frequency of contractions are known, their amplitude and the resting tone of the uterus cannot be measured accurately by external means. Again it is difficult in a particular record to evaluate the degree of inco-ordination and assess its importance.

Nevertheless in 64 cases (49 primiparae, 15 multiparae) in which mechanical difficulty could be excluded and in which it was possible to obtain continuous records for three hours or more in the first stage of labour, the necessary data were examined. Two estimates of uterine work or activity were considered: (1) the average number of contractions per hour and (2) the average duration of a state of contraction per hour. Records were arbitrarily classified into those showing "normal", "minor inco-ordination" and "major inco-ordination" patterns. The rate of dilatation of the cervix in centimetres per hour marked the progress in labour.

The number of cases is too small for firm conclusions but the chief data are presented in Table I. No direct relationship could be deduced between the intensity of the uterine activity or the degree of co-ordination as recorded and the rate of progress in labour. Thus, among the primiparae, the contraction rates in the "normal" and "prolonged" groups were almost the same.

TABLE I

	Primiparae Normal Labour.	Primiparae Prolonged Labour	Multiparae Normal Labour
Total	36	13	15
Motility Pattern:			
Normal	11	2	6
Minor inco-ordination ..	21	8	9
Major inco-ordination ..	4	3	0
Number of contractions per hour	19·6	20·2	17·0
Dilatation of cervix in cm. per hour	0·92	0·28	1·38

It may occasion some surprise to note that in more than half the cases the contraction pattern showed "minor inco-ordination"; but this investigation has served to confirm a clinical impression that labour is sometimes short and easy despite irregular contractions, while it may be prolonged when contractions are strong and regular. Among the normal primiparae, for example, the rate of dilatation was actually higher in cases showing a "major inco-ordination" pattern than in those with "normal" co-ordination. The most obvious—and expected—feature was that in most multiparae dilatation of the cervix was more rapid than in primiparae. Yet there was no significant difference in the contraction rate, and indeed (so far as can be judged from external records) in multiparae the amplitude of contractions was much less; in other words, the expulsive forces were much weaker.

In another approach to the same problem, an attempt was made to correlate the functional activity of the uterus as revealed by external tocography with the morphological state of the cervix at the time of surgical induction of labour. The view may not receive universal acceptance but there is a considerable body of evidence that the success of surgical induction depends on the "ripeness" of the cervix. In a separate investigation in this Department for example (Moir, 1956) it was found that when the cervix was favourable the operation was successful in 96 per cent of cases, but that when

the cervix was unfavourable the success rate fell to 63 per cent. If the functional behaviour of the uterus after surgical induction depends on the anatomical configuration of the cervix, then, conversely, it might be expected that the degree of "ripeness" of the cervix would be proportional to uterine motility before operation. This has not been confirmed in an examination of 37 cases. The functional activity of the uterus as estimated from external records (of two hours' duration or more) taken the day before surgical induction bore no relationship to the state of the cervix.

Comment

The multichannel Hydroflex external tocograph is a convenient means of recording the motility of the human uterus synchronously from several points on the abdominal wall with the aim of studying the details of the contractility pattern.

The efficacy of the method is represented by the number of cases in which, with surprising exactitude, an external tocographic record will parallel a tracing of intra-uterine pressure. This, too, is the finding of other investigators using different methods of external tocography. Indeed Smyth (1957) claims that an external tocograph which he has recently described will—at least in certain circumstances—give an accurate measure of intra-amniotic pressure.

While confirming its merits the present investigation, however, has shown the limitations of the method and has defined some of the possible sources of error in the interpretation of results. In particular, it has shown that the records produced by an external tocograph are influenced both by the extra-uterine soft tissues and the uterine contents. The effect of these extraneous factors is to influence and modify both the resting "tone" or base line in the record and the amplitude of contraction peaks, with obvious implications in so far as the reading of multichannel records is concerned.

In addition to these fallacies one other at least requires mention. Temporary variations in the pattern of a tocographic record are common (Embrey, 1955b), e.g., temporary phases of incoordination in an otherwise co-ordinated record and spasmodic deviations of preponderance in a record showing mostly dominance in one channel.

The records obtained show an *overall* pattern characteristic of the individual case, which has to be studied *as a whole* if serious errors of interpretation are to be avoided. As with other methods of tocography all the records obtained with the Hydroflex recorder are characterized in pregnancy, labour and the puerperium by recurring waves of contraction, each contraction mounting in a fairly abrupt systole to an acme which is sustained a short time to be followed by a more gradual diastole. In pregnancy the contractions (Braxton Hicks' contractions) are infrequent, every 15 or 20 minutes, but they are of the same order of amplitude and duration and closely resemble those of labour. The contractions of labour commonly last ½ to 2 minutes and their frequency normally varies from 2 to 5 minutes.

In a surprising proportion of normal labours a tocographic record reveals some irregularity or inco-ordination in the frequency, duration and amplitude of contractions. The present investigation has not corroborated the customary assumption that co-ordination or regularity of the contractility pattern is an essential requisite for normal labour and that frequent and powerful contractions make for rapid progress. It has not been possible to relate the rate of progress in labour either to the amount of work done by the uterus or the degree of co-ordination in contractility record. Progress may be rapid with weak and irregular contractions while labour may be slow despite strong contractions. These observations suggest that the degree of resistance offered by the cervix (and possibly the pelvic floor) may be of more importance in determining the rate of progress in labour than the strength and character of the uterine contractions.

This study has revealed that almost invariably multichannel records in normal pregnancy and labour exhibit a remarkable degree of co-ordination or synchronization between the upper, middle and lower uterine zones. While on occasion the contraction wave in one or other channel appears to precede its neighbours by a few seconds, the overall picture is one of close synchronization in the three channels, as seen in the records presented. The notion that

the uterine contraction is peristaltic has a good deal to commend it, but unlike Karlson (1949) I have not been able to demonstrate a definite peristaltic pattern of contractility as characteristic of rapid labour. The speed of the tocograph is such as to make very small differences of timing difficult to demonstrate graphically, but it can be said with some assurance that if the uterine contraction is initiated in a "pacemaker" its speed of propagation is very rapid.

Whereas Reynolds *et al.* (1948a, b, 1954) maintain that the intensity of the uterine contractions in the upper, middle and lower segments normally shows a descendent gradient, this phenomenon has not been demonstrated in the present investigation; subject to the influence of extraneous factors the records obtained usually show mid-zone dominance. The descendent gradient of intensity of Reynolds *et al.* is, of course but one feature of the "triple descendent gradient" of Alvarez and Caldeyro-Barcia (1954), who claim that the normal uterine contraction is also characterized by a descendent gradient of duration and is transmitted as a wave with downward propagation.

Somewhat inexplicably they do not appear to regard the latter as amounting to peristalsis except in the puerperium. This opinion seems to be based on the observation that the rate of propagation is four or five times faster in labour than in the puerperium; but, remembering the retraction of the uterus which has occurred meanwhile, this difference of speed must surely be expected, whereas the notion that the whole character of uterine function changes with the expulsion of the child seems unlikely.

The representative opinions on uterine motility quoted illustrate the trend nowadays to modify the traditional conception of an actively contracting and retracting upper segment and a passively distending lower segment and, instead, ascribe to the cervix and lower segment a particular dynamic quality.

While it has been argued on theoretical grounds (Halliday and Heyns, 1952) that the traditional view is not untenable, there is much which is attractive in the modern concept of fundal dominance and a descendent gradient of uterine activity from fundus to cervix, and a large body of opinion supports it. It should be pointed out, however, that much of the evidence on which it is based comes from studies of multichannel external tocography, the results of which—unless regard is paid to the limitations of the method—can be fallacious. In this connexion, one particular misconception is all too common. Considerations of topographical anatomy must leave one in considerable doubt whether—as has been frequently presumed in such studies—the activity of the lower segment can be recorded at all by external tocography. Certainly nothing of the behaviour of the cervix can be revealed by such means.

Work carried out with the Hydroflex external tocograph has not produced any tangible evidence demanding a departure from the traditional views about uterine contractility. The bulk of the evidence derived from this study of external tocography indicates that the normal contraction (even if initiated in a pacemaker) quickly spreads to involve the whole of the upper segment synchronously in a progressive sequence of systole, acme and diastole of contraction. The behaviour of the lower segment and cervix meantime may well be of fundamental importance in determining the progress of events in labour, but this cannot be revealed by external tocography.

Summary

(1) An extended trial has confirmed that external tocography provides a convenient and in many ways valuable means of recording uterine motility in pregnancy, labour and the puerperium.

(2) The records, however, have been shown to be influenced both by the abdominal parieties and by the uterine contents and possible fallacies in the interpretation of results have been demonstrated.

(3) It has not been possible to correlate the rate of progress in labour either with the intensity of uterine contractility or with the pattern of uterine motility. It may be that the degree of resistance in the cervix and lower segment of the uterus is of more importance than the strength or regularity of contractions in determining progress in labour.

ADDENDUM

The multichannel external tocograph used in these studies is now manufactured by H. G. East & Co., 37a Cowley Road, Oxford, under the name of the "Oxford" Tocograph.

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CERVICAL INCOMPETENCE AND HABITUAL ABORTION*

BY

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INCREASING interest has been taken in the subject of incompetence of the cervix as a cause of habitual abortion over the last few years by the publication of a number of papers, particularly that of Lash and Lash in 1950. More recently McDonald (1957) has published his experiences with a larger series of cases in Melbourne. There may be such a thing as congenital, physiological, or functional incompetence, but the condition under consideration here is a mechanical or structural deficiency, secondarily acquired by forceful disruption during abortion, dilatation, high amputation, Caesarean section, or trauma during vaginal delivery.

The condition manifests itself by a sequence of abortions in the mid-trimester, often at about 20 weeks of gestation. The onset is liable to be sudden with rupture of the membranes, and the abortion rapidly completed. Preceding bleeding, such as would suggest disturbance of the placental site, or labour pains from neuromuscular action, is unusual, although there may be preliminary seepage of fluid, a feeling of pressure in the sensitive lower vagina, or the bag of membranes may present at the vulva.

Diagnosis is best confirmed immediately after delivery by exploring the canal with the finger, when the deficiency may be felt in the midline anteriorly, or laterally often to the left. In the involuted uterus, a sound may be freely moved transversely across the internal os, or an 8 mm. dilator may be passed without resistance. Hysterogram on occasion may show the outline of the canal to be uniformly widened like a sleeve, instead of the usual fir-tree appearance (Fig. 1). The radiographic appearances of the cervix are very unreliable although attempts have been made by Hunter, Henry and Heinicke (1957) to dissolve the tenacious mucus in the canal and give a better outline.

In the first trimester, the uterus is protected in the bony pelvic basin, the amniotic sac is small in comparison with the fleshy contents, it does not fill the uterine cavity, and it is under no appreciable tension. When the uterus rises into the abdomen, the thinned-out membranes are applied over the os, and the cystic sac is hugged by the contractions of Braxton Hicks. When the cervix is incompetent, examination with the finger early in the second trimester will often show the bag of membranes to be palpable like those of a multipara at term. That abortion does not occur inevitably and at once, is contrary to the usually accepted law of polarity of the uterus as we think of it in relation to inevitable abortion.

MECHANICAL PRINCIPLES

The condition is best understood from a consideration of the hydrodynamic principle involved in such a system. According to Pascal's Law (or paradox), the pressure at any point in a liquid depends on the depth or height of the liquid irrespective of the shape of the container (Fig. 2). If pressure is applied to a liquid, in a

PASCAL'S LAW

FIG. 2

The pressure at any point P in a liquid is proportional to height of fluid above, irrespective of the container.

* Read at Fourth Conference in Australia, Royal College of Obstetricians and Gynaecologists, 28th August, 1957.

J. Vet. Med.

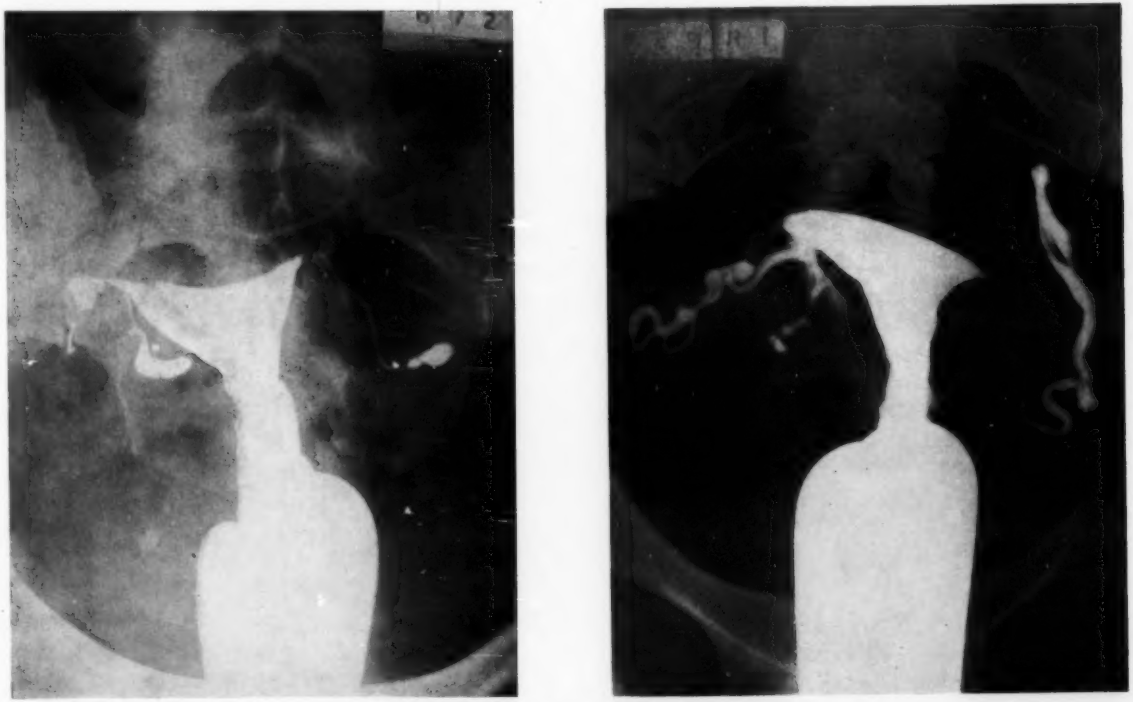

FIG. 1

Hysterograms to show sleeve-like outline of the cervix in incompetence, instead of the more usual fir-tree appearance.

FIG. 6

Radiograph to show tantalum wire loop surrounding the outer shell of the upper cervix in a case in whom five mid-trimester abortions had occurred previously, during two of which purse-string sutures had been attempted.

closed system, then this is transmitted equally throughout to all points. The pressure at the cervix is thus the resultant of the weight of liquid above, together with the pressure transmitted through it from the muscular wall of the uterus, and any positive or negative extrinsic pressure in the abdomen (Fig. 3).

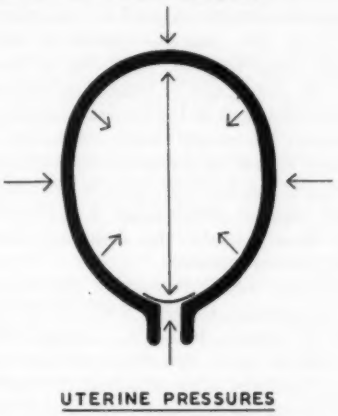

FIG. 3

The pressure at the cervix is the resultant of the height of liquid above, together with the pressure transmitted through it from the tension in the muscular wall, and any positive or negative extrinsic pressure in the abdomen.

When the cervix is open, the important factors are three in number: the size of the opening, the strength of the covering membrane, and the forces which act on its surface. Let us consider a fixed circular opening with a pressure P applied to all parts of the surface (Fig. 4). As P increases, the membrane will be forced through the opening and will take up successive positions as shown. In each position, the shape will be part of a sphere, and, as the pressure increases, the radius of the spherical section gets smaller and smaller. The smallest possible radius of the sphere is the radius of the opening, and the expanded membrane is then exactly a hemisphere. At all times, the difference in pressure P on the two sides of the membrane will be related to the radius of the spherical section by the "spherical pressure vessel" relationship of Laplace, $P=2T/R$ or $T=PR/2$, where T is tension in the membrane and R the radius of spherical section.

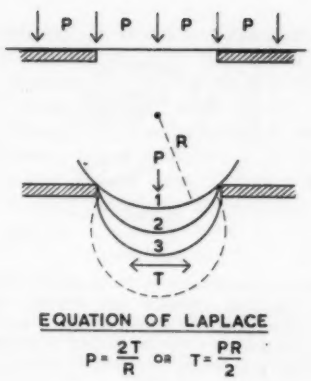

FIG. 4

A pressure P applied to a membrane covering an opening will cause the membrane to bulge and set up a tension T in the membrane. As P is increased, the protruding sac will take up successive positions, which are segments of a sphere of diminishing radius R. The critical point is reached when the section is hemispherical and the radius of the sphere equals the radius of the opening. The three variants are correlated in the relationship of Laplace.

If the inside pressure is maintained or increased, then the bulge will be greater than a hemisphere and will now have a greater radius. This means that the tension in the membrane is now insufficient to withstand the pressure, and the bulge enlarges indefinitely until either the membrane breaks or the pressure inside is deflated. It is of course quite possible that the membrane may not be strong enough to reach the hemispherical stage, but this hemispherical stage is the critical one beyond which the bulging will increase unless the pressure is decreased. That is, for a given pressure and tensile strength of membrane, there is a critical size of opening. This phenomenon will be familiar to those who have watched the herniating blow-out of a balloon tyre. Looked at in another way, to produce the critical bursting tension in a given membrane, the extruding pressure and the radius of the orifice of herniation may vary inversely to one another according to a hyperbolic curve (Fig. 5). Great pressures will extrude a given membrane through small holes, and large holes will support only low pressures.

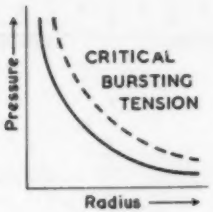

FIG. 5

To maintain a fixed tension in the membrane in a system such as described, Pressure and Radius may vary according to a hyperbolic curve; or the critical bursting tension of a membrane may be reached by combinations of pressure and radius according to such a curve.

Applying the equation T=PR/2 to the uterus, it is obvious that there is a bursting tensile strength T of the membranes which is fixed and not capable of therapeutic alteration. Values of this for membranes at term were worked out by Matthews Duncan in Edinburgh 90 years ago and more recently by Danforth, McElin and States (1953, 1956) in America, and Embrey (1954, 1956) in England. Much work has been done on intra-uterine pressures in labour at term by Carey and others, but I am not aware of the normal variations in the mid-trimester. It would seem likely that the resultant pressure at the cervix would be progressively increased during pregnancy, both from increasing uterine tone, and depth of liquor. From my observations it is rare for the membranes to be so weak that they give way when the bulge is lenticular, and before the critical point is reached when the spherical radius reaches that of the aperture. Once this is reached, the progressively expanding sac takes on a sausage-shape, modified by the conformity of the upper vagina, and the effect of gravity. The friable external chorion is the first to go, after which there is seepage of fluid for, unless protected by the chorion, the amnion is capable of secreting in both directions (thus accounting for many of the cases of prolonged leakage in ordinary obstetrics). The condition being dependent on mechanical factors, there is a latent interval before contractions ensue as a result of muscular retraction of the uterus and reflex distension of the vagina.

TREATMENT

The theoretical considerations already outlined make a proper selection of cases, where the aetiological factor is mechanical, a first requirement. Treatment would seem to hold out little hope once the critical stage of herniation is passed, the chorion broken, or the uterus active. The pressure may be reduced by measures such as relaxing the uterus, removing pressure externally from its wall, posturing to counteract gravity, or perhaps by placing plastic moulds or hydrostatic bags in the vagina to support the membranes. It would seem that the main endeavour should be directed to determining by what means the aperture may be reduced, and at what time in relationship to pregnancy it should be executed. The following lines of treatment seem possible.

(1) Surgical repair to narrow the internal os before conception, suggests itself as the obvious method of choice. Rubovits, Cooperman and Lash (1953) have described various plastic repair procedures, after reflecting the bladder to expose the area of deficiency. This has been done by pleating the area with embrocating sutures, by excision of the area in an elliptical manner and coapting with interrupted sutures, or by a wider excision of a segment in continuity down to the external os.

The cervix is an unkind and rubbery substance, and trachelorrhaphy procedures in practice are usually less satisfactory than illustrations would imply. The upper part of the cervix is no exception, and moreover in my experience the laceration is rarely found anteriorly. It may be that the operation would best be done immediately after an abortion when the cervix is soft and gaping, rather than before conception. The following case is quoted, not as a triumph for the procedure, but to illustrate the difficulties.

Case 1. The patient, aged 37, was examined in consultation in 1951, three hours after a rapid and painless labour at 20 weeks of gestation. She had had two similar experiences at approximately the same time in pregnancy. There was a history of curettage for spasmodic dysmenorrhoea, and of termination of an unwanted pregnancy before she was twenty. She now intensely desired children.

Examination showed a soft lax cervix hanging loosely down, with an area of deficiency running up from a

laceration in the left side into the region of the lower segment. It was decided that operation would be undertaken when the tissues had involuted and were less vascular. Five months later at operation, the cervix was found to be hard throughout both lips, but there was a deep laceration on the left side extending up into a crevice on the vault, and a much more superficial notch on the right side. A sound passed easily into the uterus, and could be moved bodily from side to side, rather than rocked in the internal os.

The cervix was taken in guy-rope sutures, and the edges of the laceration excised in one large wedge extending up to include the upper cervix after the manner of very deep trachelorrhaphy of bygone days. To do this, it was necessary to extend the incision out on to the vault and raise the vaginal epithelium to define the limits of the bladder on the anterior lip. A series of interrupted through-and-through chromic gut sutures was inserted from above in the region of the supravaginal cervix downwards approximating the cervical substance, and the superficial structures then closed in the vault. The small laceration on the right side also was excised and two sutures inserted.

Access to the high and deep sutures was not easy, the cervical substance was hard to define from the surrounding insertion of the cardinal ligament, bleeding was free, and there was a lack of aesthetic satisfaction about the procedure of trying to excise and suture a laceration in such a situation. A series of secondary haemorrhages followed, with repeated packings and transfusions. The area of what was a deep laceration was eventually replaced by a larger area of scar tissue. A year later, a Rubin's test was done and the cervix seemed competent. The patient then became pregnant, remained in bed throughout, increased in weight and became oedematous in spite of treatment, and was successfully delivered at 38 weeks by Caesarean section.

(2) Another method which is possible, is the production of some degree of stenosis by scar tissue, using high and deep cautery in the cervical canal before conception. This is a method of which I have had no experience. L. C. Averill of Christchurch, New Zealand, has been favourably impressed with the method using 6 to 8 linear streaks extending well up the canal (Personal Communication). In a Postgraduate lecture at Hammersmith in October, 1951, he described 18 cases with successful pregnancies following the operation in 22 cases.

(3) The unsatisfactory nature of these procedures brings to mind the possibility of using non-absorbable material as a mechanical device to support and prevent the spread of the cervical ring, rather than to narrow and repair it. Such fixed mechanical methods must all suffer from the drawbacks of requiring either removal to allow delivery, or resort to Caesarean section. There is also the difficulty of deciding the level of the physiological internal os after formation of the lower segment, and of the material cutting through like a seton during its formation. The following case is described as an illustration of a possible method using Tantalum wire as a loop to encircle the upper cervix and give support to the aperture. I was not aware at the time that Shirodkar had used a fascial strip for the same purpose.

Case 2. The patient was aged 34 and without children in spite of 5 previous pregnancies. The first was unwanted and had been surgically terminated at 2½ months. The next two pregnancies terminated rapidly at 4½ and 5 months after sudden rupture of the membranes. With the fourth, an attempt had been made elsewhere to save the pregnancy by suture of the cervix. The history, obtained from the patient, was that there was a slight show of blood at 2 and at 3 months, after which she spent most of the time in bed. At 5 months, when standing, she felt the bag coming down, but it went back when she lay down. Her medical attendant then sutured the cervix with silk but she continued after that to drain fluid and came into labour some days later. Some manipulations under anaesthesia were necessary to correct the lie of the baby and effect delivery, and it is presumed that the ligature was divided.

She was first seen by me on 6th July, 1956, regarding future pregnancies. The cervix was found to be shortened and lacerated into a number of nodules. A sound could be passed through the canal and moved laterally from side to side. It was decided, if she became pregnant again, to suture the cervix at the fourth month as a prophylactic measure. Pregnancy accordingly occurred, the last period being 9th October, 1956, after which the patient rested and took vitamin and Ethisterone tablets. Arrangements were made for the suturing to be done on 9th February, 1957, when she would be four calendar months. Three days before that time, however, the local attending doctor was called because there was slight seepage of fluid, and he found the cervix open and the membranes protruding. Under anaesthesia, one hour later, the cervix was found to be two-fingers dilated and the vagina was partly filled with a protruding sac covered by a very thin layer of amnion and shreds of chorion. The cervix was grossly deficient, consisting of a number of ragged nodules, and the posterior lip hung down like a bucket handle, having been buttonholed as a result of suturing during the previous pregnancy. Using the Trendelenburg-lithotomy position and assisted by swabs on holders, an attempt was made to reduce the sac sufficiently to encircle the cervical stump with a silk purse-string suture. This was not possible, and finally the membranes were ruptured, thus ending the fifth pregnancy unsuccessfully at 17 weeks of gestation.

The patient was now willing to try anything so it was decided, as a prophylactic and somewhat experimental

measure, to insert a metallic suture round the cervix. On 10th April, 1957, under anaesthesia, the cervix was found to be patulous, a sound could be moved across the canal and an 8 mm. dilator passed easily into the uterus. The bladder was reflected from the anterior lip using a T-shaped incision. Although the vaginal portion of the cervix was short, and buttonholed posteriorly, there was no deficiency in the anterior lip but there was a deep laceration running high up to the left. A number 4 Tantalum wire, 0·025 inch, was passed round the upper cervix in its outer shell of substance using an appropriately sized trocar-pointed needle. It was twisted about 5 times, the ends cut short and turned down, and the wire twist flattened over. Superficial sutures were then used to close the soft tissues. The loop *in situ* soon after operation is shown in Figure 6. The patient is now in early pregnancy, having seen the last menstruation on 30th June, 1957. Should she reach viability Caesarean section will probably be undertaken, although an inevitable abortion would necessitate removal of the wire, and would be a disadvantage.

(4) The last line of treatment to be considered is closure of the cervix after conception but before the abortion is inevitable. This has usually been done using a purse-string of silk as advised by McDonald of Melbourne in his large series of 70 cases. Other devices suggest themselves, such as mattress sutures of nylon, perhaps braced with plastic to prevent cutting through. In my own experience this has been difficult, and, after a number of unsuccessful attempts such as the one already described, I have concluded that the attack has been left too late in pregnancy. If the critical point has been reached, although the patient may not be in labour, the mechanical difficulty of reducing the herniating and expanding sac and retaining it with a reasonably high purse-string, can be most troublesome. It would seem better to examine the patient digitally each week, or, if the history is sufficiently clear-cut, to insert the suture early in the second trimester. Although there is no history of previous cervical trauma to account for a mechanical defect, the following case serves as an illustration.

Case 3. The woman, aged 29, had four previous pregnancies with one surviving child. She lost the first at 21 weeks of gestation 5 years previously. The labour was said to have been rapid but was preceded by some vaginal bleeding. During the next three pregnancies, she was attended by my associate, Dr. K. B. Layton. In the first of these, she rang at 24 weeks to say there was a sense of fullness in the vagina and she could feel the baby kicking on the rectum. The vagina was found to be filled with the protruding sac which remained until the next day when termination occurred. The patient in the next pregnancy decided to retire absolutely to bed, and with this regime and progesterone treatment she carried to 34 weeks and was then delivered of an infant which survived. She then became pregnant for the fourth time but remained ambulatory. At 21 weeks while standing in the garden, she felt something give way. Movements were then felt low down on the pelvic floor as on a previous occasion, and there was a sense of pressure in the region. She was put into hospital for consideration of suturing the cervix but the sac and foetus were visible at the outlet and this was mechanically not possible.

She became pregnant with the last menstrual period on 24th November, 1956, and it was decided to suture the cervix prophylactically. This was done on 31st March when she was 18-weeks pregnant. The cervix was patulous but there were no actually bulging membranes. There was no difficulty in inserting a purse-string suture of Number 5 silk around the upper aspect of the vaginal portion of the cervix taking a series of bites into the vaginal mucosa at its junction with the cervix. This was drawn comfortably tight and knotted in front, the ends being left long and knotted together, but not sufficiently to protrude from the vulva. The patient was given sedatives and chemotherapy and then allowed to walk about. She remained well without undue discharge or bleeding and was seen each week. The suture was divided two weeks ago somewhat before term, and she was successfully delivered of an infant the next day, which is surviving. The long ends of the suture were used as a guide to find the purse-string, which was buried in the vascular and oedematous cervical tissue but there was surprisingly little inflammatory reaction. It is suggested that the successful result was due to insertion of the suture prophylactically before the herniation became progressive.

Summary

(1) The condition of incompetent internal os is briefly outlined.

(2) The hydrodynamic principles are discussed.

(3) Consideration is given to the possible lines of treatment.

(4) A Tantalum wire loop is suggested as one means of supporting the cervical aperture.

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VAGINAL HYSTERECTOMY

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JUDGED by the literature that has appeared on this subject, and by the opinions expressed in conversation by gynaecological surgeons of the British Isles, there would appear to be still a lack of enthusiasm for the operation of vaginal hysterectomy.

Green-Armytage reported in 1939 that from 1902 to 1939 only 16 British surgeons had recorded cases in the British *Journal of Obstetrics and Gynaecology* and that vaginal hysterectomy had been a subject for discussion only once in the preceding 24 years at the Royal Society of Medicine. Since then only one further record of cases of vaginal hysterectomy performed by a British surgeon (Burke, 1950) has appeared in the Journal and only one discussion on this subject has taken place at the Royal Society of Medicine (Howkins, 1948; Palmer, 1948). Thus it has been before the Society for consideration and review only twice in the past 56 years.

There are centres in this country where vaginal hysterectomy is not performed and other centres where it is but an occasional operation. The varying incidence is well illustrated in the following tables—the first shows the number of hysterectomies performed in six teaching hospital units in recent years, and the second shows the number performed during 1956 in various centres of the Oxford Region.

It is difficult to explain why the incidence varies from 1·6 to 48·5 per cent of vaginal hysterectomy in the above hospitals which are fairly representative of hospitals in this country. Possible explanations are that accepted indications for the operation in one centre are unacceptable in another, or that the operation is neither sound nor safe, or that there are too many post-operative complications. In order to see how far these considerations might apply the first 1,000 operations of vaginal hysterectomy performed in the Area Department of Obstetrics

TABLE I

Hospital	Year	Abdominal Hysterectomy (including Wertheim's Hysterectomy)	Vaginal Hysterectomy	Per cent
Guy's	1955	118	2	(1·6)
Royal Infirmary of Edinburgh	1956	214	37	(14·7)
St. Bartholomew's	1955 1956	372	53	(12·4)
University College	1956	97	13	(11·8)
Royal Infirmary (Glasgow)	1956	89	15	(14·4)
Victoria Infirmary (Glasgow)	1956	113	17	(13·0)

TABLE II

Incidence of Vaginal Hysterectomy in Oxford Region, 1956

Area	Abdominal Hysterectomy (including Wertheim's Hysterectomy)	Vaginal Hysterectomy	Per cent
Aylesbury, Amersham and High Wycombe	163	3	(1·8)
Reading	198	21	(9·6)
Northampton—Kettering	350	72	(17·0)
Nuffield Department (Oxford)	104	12	(10·3)
Area Department (Oxford)	231	218	(48·5)

and Gynaecology at Oxford between the years of 1943 and 1956 have been reviewed. All cases have been included and they represent the work of a team for the operations were performed in some instances by senior housemen or registrars under supervision and in others by the consultants of the Unit.

The records of the patients have been studied in detail. A 6-weeks post-operative examination was carried out in 944 patients. A long-term follow-up of one year to seven years has been completed for over 400 patients.

MORTALITY

There was only one death in the 1,000 cases, a mortality of 0·1 per cent. This was a woman of 67 years (Mrs. E.B.) who became mildly cyanosed during the course of the operation, which was being performed under a spinal anaesthetic. Her colour never recovered completely despite therapeutic measures and she died 28 hours after operation. No cause of death was found at autopsy. The pelvic ligatures were firm. There had been no abnormal blood loss during operation, nor subsequently.

As the operations in the series under review were performed by a variety of surgeons of varying experience this low mortality figure of 0·1 per cent would suggest that the operation, with reasonable care, is a safe procedure.

A comparison of the mortality rates from various surgeons all show low mortality figures (Table III).

These results over the years support the view that the operation of vaginal hysterectomy carries with it a low mortality.

TABLE III

Mortality in Vaginal Hysterectomy

Name	Year	Number	Died	Percentage Mortality
Phillips, Miles	1934	660	13	2·96
King, W. W.	1934	539	12	2·2
Datnow, M.	1934	196	3	1·5
Price, J.	1944	More than 4,000	a fraction of 1	
Green-Armytage, V. B.	1939–1954	2,000	12	0·6
Burke, F. J.	1950	585	3	0·5
James, J. R. E.	1952	368	1	0·27
Counseller, V. S., and Hunt, W.	1954	2,867	1	0·03

Morbidity

A patient was considered to be morbid if her temperature was elevated to 100° F. on two consecutive days in the post-operative period (that is, until she was discharged from hospital). Three hundred and twenty-three patients, 32·3 per cent, came into this category, and in 46 per cent of these no specific cause was found for the mild pyrexia which subsided without treatment within a few days.

Patients are admitted two days before operation, and on the following day are given a thorough shave followed by an enema and a bath. Immediately before operation the vulval area is washed over with a weak dettol solution and then cleaned with cetavlon solution from the umbilicus back to the buttocks and down the thighs, and covered with a sterile pad and towel. The vaginal and vulval toilet is completed in the operating theatre with flavine in spirit.

Where ulcers have formed in the vagina from the wearing of ring pessaries or from external pressure in a procidentia preliminary vaginal packing is carried out with gauze soaked in flavine emulsion, often combined with oestroform pessaries. Antibiotics are not used before operation and only afterwards where indicated.

Pratt and Scherman (1954) claim to have reduced the morbidity rate to 20·4 per cent in 514 vaginal hysterectomies at the Mayo Clinic by the insertion of a suppository containing 100,000 units of penicillin into the vagina the night before operation and 5 grams of sulphathiazole into the peritoneal cavity at operation. The standard of morbidity in these cases was a temperature of 100·4° F. for two or more days after the first 24 hours following surgery.

In the series under review sepsis however has not been a major problem. Sixteen cases of pelvic cellulitis and 5 of pelvic abscess were recorded. The latter arose from infection occurring in a pelvic haematoma. In all cases resolution followed spontaneous discharge of the infected haematoma through the vaginal vault. In no patient was it necessary to open and drain a pelvic abscess. The haematoma has been always extraperitoneal, and any sepsis therefore has been outside the peritoneal cavity. Consequently none of these patients developed ileus or vomiting.

It is our contention that these haematomas (and hence abscesses) should not occur for they are the result of imperfect haemostasis. It has long since been recognized that reactionary haemorrhage means bleeding resulting from failure to secure pedicles properly and imperfect ligature of bleeding points. It should not, therefore, occur.

The main cause of post-operative morbidity has been urinary infection (158 cases, 15·8 per cent).

As nearly all the hysterectomies have been combined with some form of plastic vaginal repair a self-retaining catheter has invariably been inserted into the bladder at the conclusion of the operation. Many of the patients (see later) had a repair for stress incontinence of urine. There has often been a delay of some days before the resumption of spontaneous micturition. This difficulty and the in-dwelling catheter necessarily lead to urinary infection but with the judicious use of alkalies, sulphonamides and antibiotics the infection has not been a serious problem. Sometimes it was a problem to maintain the patient's morale and to assure her that she would be able to "pass her water naturally again". In no case was there a vesico-vaginal, ureteric or recto-vaginal fistula following the operation.

Complications

Haemorrhage

Apart from what has already been said in relation to sepsis, haemorrhage has not been a problem. Twenty patients had a secondary haemorrhage which was treated satisfactorily by a hot douche alone, or by a hot douche and vaginal pack for 12 to 24 hours or by a hot douche together with ligature of a bleeding point. In the whole series, for varying degrees of blood loss at operation, or for secondary haemorrhage, blood transfusions were necessary in only 16 patients. A pre-operative haemoglobin level of at least 75 per cent was considered essential prior to operation and iron therapy was frequently commenced in the out-patient department. If the haemoglobin was not at the desired level on admission to hospital a pre-operative blood transfusion was given.

Operation during or near menstruation was avoided.

Provided these simple rules are observed and great care is taken to secure pedicles firmly (see operation technique) blood transfusion during or after operation should seldom be necessary. Taylor *et al.* (1954) reported in 163 consecutive vaginal hysterectomies blood transfusion was required in 88 of the cases. They state "most patients receive a 500 c.cm. blood transfusion during the operation". We have not found it necessary to transfuse during operation and, as mentioned already, only 16 of the 1,000 patients required transfusion after operation.

Enterocoele

The incidence of enterocoele subsequent to vaginal hysterectomy can only be determined by a long-term follow-up. A post-operative examination at 6 weeks gives no indication of this problem for it is usually in the first six months that the enterocoele occurs but often not until after a year or more.

In this series a 6-weeks follow-up was carried out on 944 patients and only 3 had enterocoeles causing symptoms requiring subsequent operation. Four hundred and sixteen patients were examined at one year and more and there were 26 enterocoeles, which caused symptoms requiring repair.

There are few reports of long-term follow-up examinations of patients who have had a vaginal hysterectomy performed more than one year previously. It is for this reason, the authors feel, that many surgeons have asserted that post-operative enterocoele in their experience is not a problem. Gray Ward reported, however, in 1936 at the British Congress of Obstetricians and Gynaecologists in Belfast, that he had performed 82 Mayo operations between 1918 and 1934 and that enterocoele had developed post-operatively in 15, or 18·2 per cent. In the first 42 operations carried out between 1918 and 1923 the incidence of post-operative enterocoele was 25·5 per cent, whereas, in the second 40 between 1923 and 1934, the incidence was 10·0 per cent (after using an improved technique of obliteration of cul-de-sac and suturing utero-sacral ligaments).

Although this subject had been under consideration for some time in the Department our interest was further stimulated by a paper given by Mr. L. A. Cruttenden at the Birmingham and Midland Obstetrical and Gynaecological Society in 1953 in which he reported a 6 per cent incidence of vault prolapse causing symptoms after vaginal hysterectomy.

The extent of the problem was not fully appreciated by us until 246 cases were re-examined at more than one year, having had a routine examination at six weeks. This survey was carried out by Mr. C. Simmons in 1953. He reported that there were 18 cases in the series of 246 who had had a subsequent enterocoele repaired and there were 3 more giving symptoms requiring operation, and 20 with a "bulge" of greater or lesser degree at the vault of the vagina on straining which was symptomless.

Thus there were 21 cases of enterocoele requiring subsequent repair in 246 cases operated on more than 1 year previously—an incidence of 8·5 per cent. In view of this various procedures were adopted to try to overcome the difficulty.

One of us (W.H.) was of the opinion that the fascia of the pelvic floor provided the answer to the post-operative enterocoele, and commenced carrying out a high fascial repair above the level of the levatores ani muscles, when performing the colpo-perineorrhaphy, after the uterus had been removed and closure of the vault and anterior colporrhaphy had been completed. It had been noted on numerous occasions during a colpo-perineorrhaphy that the floor of the pouch of Douglas was clearly exposed beneath the posterior vaginal mucous membrane at the vault of the vagina. This frequently presented as a downward bulge and, being the lowermost point of the pouch of Douglas, was the obvious starting point of herniation, i.e., of every post-operative enterocoele.

In the treatment of herniae in other regions of the body adequate re-suturing of the fascia had always been an essential step in the repair. It was felt that the same principles should apply in the treatment of a hernia of the pouch of Douglas. For this reason pre-rectal fascia was sutured across below the pouch and continued as a shelf by the insertion of interrupted catgut sutures

down to the point where the levatores ani were brought together by a further series of three interrupted sutures (see operation details). Thus a shelf of fibromuscular tissue was constituted from the vault of the vagina to the perineum making the formation of any subsequent hernia virtually impossible. The hernial sac was of course previously excised, where necessary, at the completion of the hysterectomy (see operation details).

In a series of 50 cases followed up in May, 1954 by one of us (J.R.) operated on more than one year previously using this technique there was no case with an enterocoele causing symptoms.

A further 50 cases, all operated upon more than one year previously by one of us (W.H.) using the high posterior fascial technique, have been followed up by an independent observer (Mr. A. MacFarlane—a visiting consultant gynaecologist from Auckland). None of these was included in either of the two previous series.

Thus 100 patients in whom a high posterior fascial repair was performed have been followed up independently (not by the surgeon) more than one year after operation. In not one of these patients has there been a post-operative enterocoele causing symptoms requiring a subsequent repair. It would seem reasonable to suggest, therefore, that by this method of repair the elimination of pouch of Douglas hernia following vaginal hysterectomy is possible. No doubt there are many other methods of securing exactly the same result. It must be re-emphasized, however, that it is not possible to come to any

TABLE IV

Indications, Age Group and Parity

Age in Years	No.
Under 35	6
35–39	84
40–44	260
45–49	276
50–54	159
55–59	140
60–64	61
65–74	61
75 and over	12
Not stated	2
	1,000

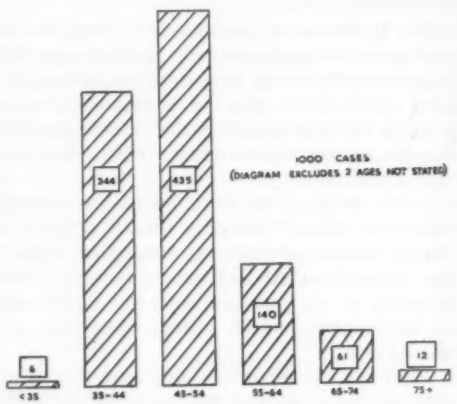


FIG. 1

Vaginal hysterectomy. Distribution of cases by age group.

TABLE V

Parity and Miscarriages

Parity	Miscarriages 0	1	2	3	4	Not Stated	Total
0	24	2	—	—	—	—	26
1	138	23	6	2	—	—	169
2	221	41	11	2	1	—	276
3	150	33	9	4	2	—	198
4	75	21	8	—	—	—	104
5	51	22	7	—	2	—	83
6+	86	26	12	8	7	—	139
Not stated	1	—	—	—	—	5	6
Total	746	168	53	16	12	5	1,000

reasonable opinion concerning the incidence of enterocoele or methods of treatment unless patients are examined at least one year and longer after the original operation.

It is suggested that the role of pelvic fascia is important in vaginal repair surgery. This will be discussed in more detail shortly.

Age Group, Parity and Symptoms

It will be seen in Table IV that the majority (53·6 per cent) of patients operated upon were in the 40–50 age-group. There were 73 patients over 65 and 12 over the age of 75 years. Figure 1 shows the numbers in 10-year age-groups.

The statistics in Table V are shown graphically in Figure 2.

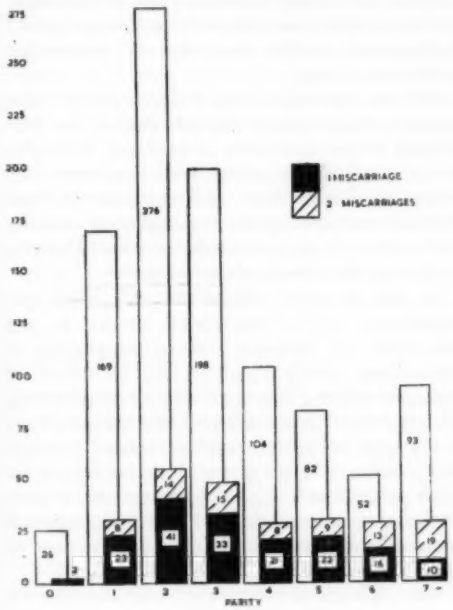


Fig. 2

Vaginal hysterectomy. Distribution of cases by parity.

As would be expected most of the patients had had either one or more children or one or more miscarriages. There were only 24 patients who had never been pregnant.

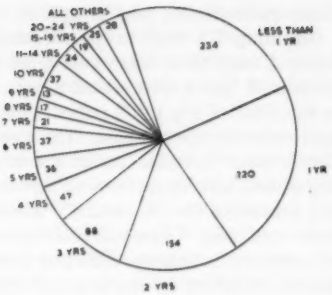


Fig. 3

Vaginal hysterectomy. Duration of original symptoms.

Table VI

Symptoms—Menstrual Irregularities

Symptoms	No. of Patients
Menorrhagia Metrorrhagia Dysmenorrhoea Polymenorrhoea Contact bleeding Post-menopausal bleeding (none due to carcinoma)	504 261
No menstrual irregularity	235
Total	1,000

Duration of Original Symptoms

Almost half the patients sought advice and were operated upon within one year of developing symptoms.

Thus in the total series of 1,000 patients there were 235 who had no menstrual disturbance as defined by the above headings. The age groups of these patients are shown in Table VII.

Table VII

Age	No. of Patients	
35–39	12	
40–44	37	
45–49	31	
50–54	45	
55–64	74	(i.e., 155
65–74	28	were 50
75+	8	or more)
	235	

Of these patients, 232 had symptoms of prolapse, including 73 with a procidentia. One hundred and forty-three were post-menopausal, and of these 30 had a retroverted uterus.

Nine hundred of the 1,000 patients had some symptom referable to prolapse. The symptoms of prolapse were included under the headings, "bearing down, something coming down, lump, dragging sensation and backache". Micturition symptoms included "stress incontinence, frequency, urgency, hesitancy, difficulty in emptying bladder, difficulty in starting and dysuria". Rectal symptoms included "rectal discomfort and/or pain, difficulty in emptying rectum, rectal incontinence and/or lack of control of flatus".

TABLE VIII

Symptoms (Other than Menstrual Irregularities)

Symptoms	No. of Patients
No symptoms of prolapse	100
Symptoms of prolapse only	151
Micturition symptoms only	123
Rectal symptoms only	13
Prolapse and micturition symptoms ..	458
Prolapse and rectal symptoms	23
Micturition and rectal symptoms	23
Prolapse, micturition and rectal symptoms	109
	1,000

Of the 900 patients who had symptoms of prolapse 426 had menorrhagia, and 242 had other menstrual irregularities included under headings, "dysmenorrhoea, polymenorrhoea, metrorrhagia, contact bleeding, post-menopausal bleeding—not due to carcinoma". Thus there were 232 of the 900 (with prolapse) who had no menstrual irregularities.

DISCUSSION

In all the 1,000 patients the indication for operation was the considered opinion that the uterus should be removed. The principal indication for its removal was some menstrual irregularity, usually menorrhagia. This was present in 765 of the patients.

If a woman, for whom hysterectomy is advised, has in addition symptoms and/or signs of prolapse then it is contended that the uterus should be removed vaginally and the prolapse repaired at the same time. Obviously this avoids an abdominal hysterectomy, combined with a vaginal repair then or later. All except 78 of the above 765 patients with menstrual irregularities had some symptom referable to prolapse. Indications other than menorrhagia for removal of the uterus in menopausal and post-menopausal patients of this series included an unhealthy cervix, procidentia and retroversion. If a patient at or around the menopause has a chronically infected eroded cervix (an unhealthy cervix) then a hysterectomy (together with a repair, if a prolapse is present) is advised. If a cervix (in this age group) is so unhealthy that carcinoma cannot be excluded except by repeated biopsies then there is no peace of mind for either the patient or the surgeon until complete extirpation of the cervix has been performed. Similarly in this age group hysterectomy is the treatment of choice for carcinoma *in situ*.

It was postulated by Palmer (1948) that vaginal hysterectomy should always be performed in the treatment of prolapse when the cervix is outside the vulva. We subscribe to this view in menopausal and post-menopausal women, emphasizing the importance of carrying out a repair of the cystocoele, pouch of Douglas hernia and rectocoele at the same time.

In 1934 Bonney pointed out the aetiological significance of a retroverted uterus in the causation of prolapse. When employing a Manchester repair alone in the treatment of prolapse we have found difficulty in overcoming a completely retroverted and retroflexed uterus —the type where the fundus presents through the posterior vaginal fornix. For this reason we have performed a vaginal hysterectomy as part of the repair in menopausal and postmenopausal patients who have a third degree retroversion as well as prolapse.

The Manchester operation is still in the opinion of most surgeons the operation of choice in the treatment of prolapse in those cases where no uterine abnormality necessitates the removal of the uterus. Whether this is true in the treatment of prolapse in the menopausal or post-menopausal woman is a matter of opinion.

The idea that the cervix constitutes the keystone of the arch in a repair is outmoded. It is a

false analogy in that the keystone in architecture depends for its importance on the rigidity of the arch. It is not possible to suspend the prolapse from the cervix. It is the uterine ligaments which are used in a Manchester repair and not the uterus itself—these ligaments are just as readily available in a vaginal hysterectomy. If the cervix were so important as a keystone of the arch then the operation of total abdominal hysterectomy would be followed by prolapse. This is not the case, unless a co-existent prolapse has been neglected. Read and Bell (1933) found none after 605 total hysterectomies but there were 4 after 1,739 sub-total operations.

In the case of a procidentia it is even more difficult to secure a high elevation of the vault by a Manchester repair, for often the uterine ligaments are grossly elongated and attenuated. The round ligaments, cardinal and utero-sacral ligaments can all be shortened, to whatever extent is desired, when a vaginal hysterectomy is performed so that when they are sutured together below the peritoneal cavity in reforming the vault a high elevation is attained. The full normal length of the vagina can thus be preserved. The vaginal fascia is more fully exposed following a vaginal hysterectomy and by careful re-suturing can be used to repair deficiencies through which an enterocoele, cystocoele or rectocoele have occurred.

Vaginal Fascia

Prolapse (apart from uterine descent) is a herniation of the bladder, or urethra or the rectum, or the pouch of Douglas through the fascia surrounding the vagina. This fascia, which normally encases the vagina, has been stretched or disrupted by childbirth, perhaps weakened by a chronic cough, or even by advancing years. Te Linde (1953) states: "however, the most important factor in the formation of cystocoele is incompetency of the pubo-vesicocervical fascia. This broad structure extends as a sheet downward from the cervix between the vaginal wall on one side and the bladder and the urethra on the other", and "posteriorly, there is also an extension of endopelvic fascia which is less sturdy than the anterior fascia but it is utilized in rectocoele repair".

This fibromuscular and connective tissue fascial layer was referred to as the "pelvic shelf" by Bonney (1934) and as a "third plane above the pelvic diaphragm" by Gray Ward (1936).

Shaw (1949) tried to separate this fascia into three components, the post-urethral ligament and the vesico-cervical ligament in the mid-line and a thicker layer of endocervical fascia on each side. Close study of his diagrams shows that the post-urethral ligament and the thickened portions on each side form one continuous sheet of fascia. This is borne out in practice. It is our contention that the post-urethral ligament is not as well defined at operation as Shaw suggests for it has been stretched and attenuated in the mid-line just as much as the rest of the pubo-cervical fascia (by childbirth, coughing, etc.) to allow the formation of a cystocoele and urethrocoele.

Referring to urethrocoele, cystocoele, rectocoele, enterocoele and prolapsus uteri, Gray Ward states: "realizing that prolapse of these various viscera is in the nature of a true hernia, the accepted principles for the correction of herniae in other parts of the body apply equally well here. The protruding viscus must be first replaced, and repair of its damaged supporting tissues must be accomplished".

The herniation usually consists of a protrusion or bulge over a wide area like a direct inguinal hernia but from time to time a patient is encountered in whom the bulge is a localized protrusion, as in a femoral or inguinal hernia. Mrs. E.C., age 60, para-4, was such a case. She had a gap or hole in the fascia beneath the bladder which would admit just one finger. When she coughed or strained a pencil like protrusion of the bladder would project itself into the vagina, much as an inguinal hernia appears on coughing. All that was necessary to effect a complete cure of this hernia was to repair the defect in the fascia.

Similarly in the treatment of a cystocoele alone, or a cystocoele together with a urethrocoele, reconstitution of the fascia beneath the bladder and urethra is the essential step in the repair. In the last 100 cases mentioned above, who had a vaginal hysterectomy and repair, operated upon by one of us (W.H.) and followed up more than one year after operation,

there has been no recurrence of cystocoele nor urethrocoele. In these patients only the fascia was united beneath the urethra and bladder. No attempt was made to secure and unite fibres of the levator diaphragm.

In cases where stress incontinence of urine is present the fascia is sutured more tightly so that a strong fascial sling is formed beneath the bladder and urethra especially beneath the bladder neck. The fascial sling so formed has almost an identical appearance and can be made just as tight as the "sling" passed beneath the urethra by one method or another of the various "sling operations".

Fifty-four of these 100 patients had stress incontinence of urine prior to operation. They were treated by re-suturing of the fascia in this way. At the one-year follow-up it was found that in 2 patients there was no improvement in the incontinence, 51 were cured and one was improved. No one procedure is likely to cure all cases of stress incontinence for the causes of the condition are many and various and moreover the exact aetiology is not yet fully understood. A follow-up examination of at least one year after operation is essential before any assessment of a method of treatment can be made.

The use of pelvic fascia in the treatment of enterocoele has already been discussed. The pre-rectal fascia is reconstituted in front of the rectum from the vaginal vault down to the levatores ani muscles, forming one continuous fibromuscular shelf the whole length of the vagina to the perineum. In the 100 cases operated upon in this manner more than one year previously there were no rectocoeles nor enterocoeles causing symptoms.

In order to obtain the maximum available fascia in either the anterior or posterior vaginal wall repair it must be dissected cleanly and freely from the vaginal mucous membrane. Also, the fascia must be freed widely. If this is not carried out with the utmost care, sutures placed laterally in the fascia will draw in the mucous membrane and produce a constriction of the vagina. (Too generous an excision of vaginal mucous membrane produces the same result.) This can occur either in the anterior or in the posterior wall repair and if in both will certainly produce a vaginal constriction usually at the junction of the lower two-thirds and upper one-third. In the earlier cases this was a major problem—in the 50 cases followed up in 1954 by one of us (J.R.) there were 10 with some degree of constriction. In the last 50 cases followed up there were 2. Enterocoele following vaginal hysterectomy could be eliminated easily by complete closure of the vagina, but unless satisfactory coital vaginal function is preserved the operation cannot be claimed as a success.

It is worth reiterating that wide separation of the fascia and carefully placed sutures are necessary to avoid vaginal constriction. Often it is a wise precaution to pull sutures tight before tying them and at the same time test with two fingers the size of the vaginal lumen. If there is any constriction the sutures should be withdrawn, replaced and tested again. This applies particularly to those sutures placed highest beneath the mucous membrane in the vault of the vagina, at the apex of the posterior repair.

This method of fascial repair is equally applicable to any vaginal repair surgery and has been used by one of us (W.H.) for the past three years in routine prolapse repair operations.

It is apparent from the foregoing statistical information and discussion that the risks and complications of vaginal hysterectomy are not great. In all surgery there is an irreducible minimal mortality from pulmonary embolism. It is interesting to note that in this series of 1,000 operations there were no deaths due to pulmonary embolus nor in a further 200 operations completed since the analysis of the "first 1,000" was commenced. Many reasons are put forward to explain the reduction in fatal cases of pulmonary embolism, such as early ambulation, the use of antibiotics, better anaesthesia and nursing techniques, the more liberal use of blood transfusion to overcome anaemia, meticulous pre-operative assessment of cases and the use of anti-coagulant drugs.

To some extent the absence of this dread complication in these cases of vaginal hysterectomy may be due to the absence of an abdominal incision which enables patients to move more easily and to breathe deeply without discomfort following operation, and to the fact that infection when present is extra-peritoneal.

Operation Technique

After a preliminary curettage, an additional volsellum is placed on the posterior lip of the cervix which is now drawn forward. Two Kocher forceps are placed posteriorly at approximately five and seven o'clock below the reflection of peritoneum of the pouch of Douglas, and a transverse incision is made connecting them. The rectal fascia and the rectum are separated by scalpel and gauze dissection from the posterior flap of vaginal mucous membrane, thus exposing the pouch of Douglas immediately behind the cervix. A Spencer Wells artery forceps is placed on the peritoneum at this point and with a pair of curved scissors the pouch of Douglas is opened. A finger is inserted to explore the posterior aspect of the uterus on either side to define the extent, if any, of adhesions. After a clean swab has been lightly packed into the pouch of Douglas to keep this area dry, the volsella are carried downwards and backwards and a Kocher forceps is placed anteriorly below the urethra. The cervix is drawn over to the patient's right side and an incision made connecting this forceps to that which was placed originally at 5 o'clock. The mucous membrane is then dissected free along this incision. The cervix is drawn over to the patient's left side and a further incision made to complete the right side of the triangle, from the sub-urethral forceps down to the forceps placed previously at 7 o'clock.

Once the mucous membrane has been dissected free along these lines the volsella are brought to the mid-line and the Kocher in front is placed on the vaginal mucous membrane just below the apex of the incision and the mucous membrane is dissected free from the fascia which is left lying on the deep surface of the bladder. When this dissection has been completed down to the cervix the bladder and the fascia are pushed well upwards to display the reflection of peritoneum of the utero-vesical pouch immediately anterior to the cervix. The peritoneum is held by a pair of Spencer Wells forceps and the pouch opened with curved scissors. The opening is enlarged by the index fingers of the two hands which are swept out and forwards on each side, and kept in the utero-vesical pouch while the assistant inserts a lateral vaginal wall retractor. This retractor is held in position throughout the entire operation so that the bladder is kept well forward.

The operation is continued by the posterior swab being removed and the index finger of the left hand being inserted into the pouch of Douglas behind the left utero-sacral ligament. The cervix is drawn well over to the patient's right side and the reflection of mucous membrane, bladder and fascia is completed on the left side of the uterus. The left utero-sacral ligament is thus displayed and is clamped by an angled Kocher forceps and then divided. It is transfixed by a number two chromic catgut ligature and knotted three times on the one side and then three times on the other side so that the pedicle is secured quite firmly. At the tying of the first knot the Kocher forceps is opened so that the pedicle can slide and then the forceps is closed again while the tying is completed. It has been found advantageous to tie the first knots on the outside of the pedicle and then to rotate the forceps outwards so that the second series of three knots can be tied on the medial aspect, the forceps being removed as the first of these three ties is made. This allows for as long a pedicle as possible to be secured.

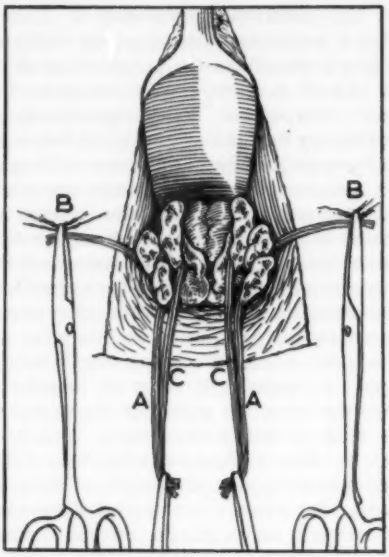
The cervix is now drawn down and over to the patient's left side and the reflection of mucous membrane and bladder completed on the right side of the uterus with the index finger of the left hand behind the utero-sacral ligament. This ligament is thus displayed, clamped, divided and ligated in a similar manner. The ends of these ligatures are left long, clamped each in a separate artery forceps, and allowed to hang downwards.

In a difficult case it is perhaps a little easier to swing the cervix back again over to the patient's right side and to deal with the left uterine artery first. The index finger of the left hand is passed into the pouch of Douglas and medial to the cut ligatured end of the left utero-sacral ligament and so beneath the left uterine artery. Once more the fascial attachments of the bladder are checked and pushed gently upwards so that the bladder and ureter are well away from the field of operation. The uterine artery is then clamped in the Kocher forceps and divided. It is secured with a number two chromic catgut ligature and

tied firmly first with three knots on one side and three knots again on the medial aspect making a double tie secured by six knots in all, so that there is no chance of this ligature slipping. Each pedicle is, of course, transfixed before the ligature is tied. This ligature is left long and is clamped separately to the drape on its respective side. The right uterine artery is then clamped, divided and ligatured in exactly the same way.

There is now left on each side only the broad ligaments to be secured. If the uterus can be made to appear easily at the vulva then it is a simple matter to clamp, divide, transfix and ligature each broad ligament in turn. Sometimes it is not possible to bring the uterus sufficiently far down to allow easy access to the broad ligaments. Under these circumstances it is a wise procedure to bisect the uterus. A volsellum is placed on each side of the external cervical os and with a scalpel the uterus is divided sagittally. There is no bleeding of moment. If there is a fibroid in the uterus or, for that matter several fibroids, they can be enucleated easily. Thus a vaginal myomectomy can be performed without difficulty allowing easy access to each broad ligament. If the broad ligament pedicle is a large one it is advisable to underpin the round ligament so that on the second tie the round ligament is secured more firmly. The ligature on each side is left long and is secured in the forceps which contains the utero-sacral ligament ligature on that side. Thus three pedicles are secured on each side of the pelvis. Those of the broad ligament and utero-sacral ligament are contained in the same artery forceps, whereas the one from the uterine artery is independent on each side and is attached to the lithotomy sheet (Fig. 4).

The next step is to close the peritoneal cavity. A Kocher forceps is placed on the distal end of each broad ligament stump and these are drawn down and slightly outwards. In order to deliver the cut edge of the utero-vesical peritoneum into the wound a small swab is placed in a sponge-holding forceps, and this swab is passed up into the peritoneal cavity and by exerting gentle pressure in a forward direction the peritoneum can slowly and steadily be brought down into view at the same time as the lateral retractor which was placed under the bladder



Ligatures on uterosacral ligaments (A)
Ligatures on uterine artery pedicles (B)
Ligatures on broad ligament pedicles (C)

FIG. 4

initially is withdrawn. An artery forceps is placed on the peritoneum, thus exposed in the mid-line, and a circular purse-string closure of the peritoneal cavity is begun, usually starting on the left side transfixing the left round ligament passing across and incorporating the cut edge of the utero-vesical peritoneum in front to transfix the right round ligament. Again in order to save pulling on ligatures two additional Kocher forceps are now placed, one on each utero-sacral ligament stump. The purse-string is continued downwards on the right side omitting the uterine pedicle passing on its medial aspect, to incorporate the right utero-sacral ligament. The cut edge of the peritoneum at the lower limit of the pouch of Douglas is secured by artery forceps so that the ligature can be continued across the posterior peritoneum at this point, usually from right to left to include the left utero-sacral ligament. The peritoneal cavity is swabbed clean of any accumulated

blood and the purse string is securely tied. This ligature consists usually of number one chromic gut.

If the patient has had a pouch of Douglas hernia the peritoneum is freed from the rectal fascia and rectum posteriorly and then closed in the purse-string at the highest accessible point. Providing all pedicles have been ligatured securely there should be no bleeding at this stage except perhaps some oozing from the small veins underneath the bladder or from the cut edges of the mucous membrane. The pedicle ligatures are cut leaving each approximately one inch long.

The vault and anterior vaginal wall repair is now begun. A long ligature of number two chromic catgut is inserted and tied at the lower limit of the vaginal mucous membrane incision. By an interlocking continuous suture the mucous membrane is closed and usually after the first or second stitch has been inserted the utero-sacral ligaments are incorporated. Usually first one and then the other, and as soon as possible thereafter the broad ligaments are transfixed in a similar manner. They are thus sutured together, utero-sacral ligament to utero-sacral ligament and broad ligament to broad ligament. No attempt is made to join them by separate sutures. Formerly this was done but no advantage was found over the method described. Once the broad ligaments have been incorporated the long suture is tied. Kocher forceps are placed on each side of the apex of the incision and if the mucous membrane has not already been divided up to the urethral meatus this is now carried out. The bladder and the vesico-vaginal fascia are separated by scalpel and gauze dissection from the mucous membrane, as far laterally as possible. This is a most important step in the repair.

When the dissection has been completed the fascia is brought together in the mid-line by interrupted number two chromic catgut sutures (Fig. 5). In this way a firm fascial sling can be constructed underneath the bladder from the region of the united upper edges of the broad ligaments up to the urethral meatus (Fig. 6). The repair of the urethrocoele, the repair of the cystocoele and the cure of stress incontinence depend upon the care that is taken in the construction of this fascial shelf. It is important that the fascia be freed laterally as far as possible for if this is not done then sutures placed widely will draw in the overlying mucous membrane and bring about a vaginal constriction. No

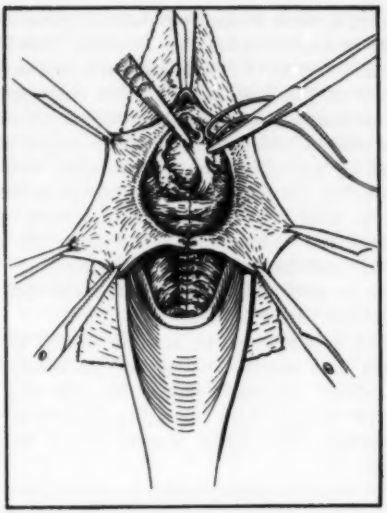


FIG. 5

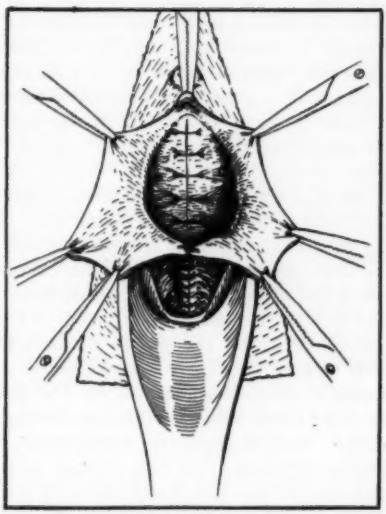
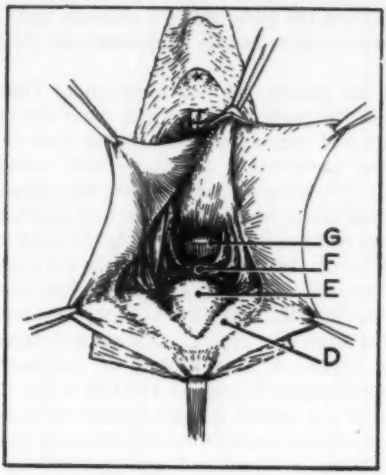


FIG. 6

attempt is made to secure pubo-coccygeus fibres of the levatores ani muscles. Provided there is no excessive oozing of blood from veins on the deep surface of the bladder no further deep sutures are necessary. Any excess mucous membrane is now excised and the anterior wall repair completed by approximating the cut edges with the continuous catgut suture. If there is excessive oozing after the fascial stitches have been inserted the venous loss can usually be controlled satisfactorily by under-pinning the vessels on each side and tying across the mid-line superficial to the fascia.

With a Sim's speculum now placed in the vagina it is possible to inspect the efficacy of the repair. The vault should be high and the anterior vaginal wall, bladder and urethra well supported. The vagina should be of normal length.

The colpo-perineorrhaphy is commenced by placing two Kocher forceps on the perineum at the muco-cutaneous junction at the posterior extremities of the carunculae myrtiformes. An incision is made joining these forceps so that the space is opened into behind the posterior vaginal wall mucous membrane and in front of the rectum. The dissection is carried upwards in this same plane to the vault, to the point of commencement of the anterior repair. The vaginal mucous membrane is divided in the mid-line and the fascia is separated widely and freely from it in exactly the same way as the fascia was separated in the anterior vaginal wall. Thus the anterior surface of the rectum is exposed and above this the pre-rectal fascia and above this at the vault of the apex of the incision the floor of the pouch of Douglas is usually visible (Fig. 7). It is at this point that a subsequent enterocoele may start. The enterocoele slides down behind and bulges through the posterior vaginal mucous membrane. It is essential, therefore, that this critical point be closed over by as much fascia as can be secured by passing deep sutures laterally to pick up the fascia above the level of the rectum on each side and then tied in the mid-line. These sutures are apt to constrict the vagina and therefore it is important first of all to secure wide separation of the fascia, and secondly to test the ligatures before tying. If constriction is produced then



Levatores ani muscles	D
Rectum	E
Pre rectal fascia	F
Floor of Pouch of Douglas	G

FIG. 7

these sutures have to be withdrawn, re-inserted and again tested before tying. These interrupted sutures, uniting the fascia beneath the pouch of Douglas and continued down, over and in front of the rectum, bring about the formation of a firm fibro-muscular shelf down to the level of the levatores ani muscles which are secured in the mid-line by three interrupted catgut sutures (Fig. 8). The uppermost of these three sutures should be placed as high as possible. The fibro-muscular shelf thus formed is continuous from vaginal vault to perineum.

The repair is completed by uniting the posterior vaginal mucous membrane in the mid-line after any excess has been removed by a long continuous running suture down from the vault to the perineum. Sometimes a few superficial sutures are necessary to bring together the superficial perineal muscles and the incision in the perineum is closed by a subcuticular, interrupted or continuous suture.

Examination should now show a long perineum, a long vagina which readily admits two fingers and which with the patient in the

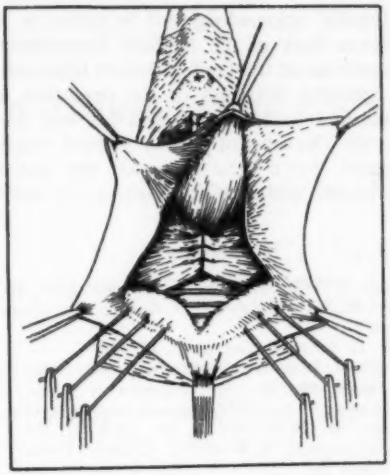


FIG. 8

lithotomy position points downwards and backwards at an angle of 70° to 80° to the horizontal. A self-retaining catheter is inserted into the bladder and the vagina is loosely packed with flavine gauze soaked in paraffin emulsion to facilitate its removal in twenty-four hours time. After the patient has recovered from the anaesthetic she is given deep breathing exercises and instructed to move her legs and turn from side to side in bed. She gets up and walks round her bed on the first day after operation and thereafter is encouraged to walk at least twice a day. The catheter is removed on the fifth day and she is ready for discharge to a convalescent home as soon as normal micturition is resumed and she has a residual urine of one ounce or less. The patient leaves hospital, therefore, 7–10 days after operation.

CONCLUSIONS

Vaginal hysterectomy is a safe procedure, devoid of distressing complications. Cofer (1946) states: "the mortality of vaginal hysterectomy is extremely low and cannot be equalled by any abdominal operation". The results presented here, 1 death in 1,000 consecutive cases, support this view.

The operation should have a place in the armamentarium of all gynaecological surgeons and it may be that vaginal hysterectomy combined with colporrhaphy will supersede the Manchester operation, in menopausal and postmenopausal women complaining of prolapse.

The cervix is not the keystone of the arch in a repair operation. The success of the repair depends on proper use being made of the ligaments and fascia. It is these that support the vault and not the uterus. It is the fascia that supports the bladder and the rectum.

A cystocoele and a rectocoele are essentially herniae of adjacent organs through the fascia which surrounds the vagina. As in the repair of herniae elsewhere in the body the essential step is replacement of the protruding viscus and repair of this fascia. It would seem unnecessary to bring together in the mid-line (other than to give additional support), fibro-muscular tissue lying beneath and deep to the ischio-pubic ani, often described as pubo-coccygeus fibres of the levatores ani muscles. These muscles do not provide the direct support of the herniae, as postulated by Pacey (1949). They serve to close the vagina and through their sphincteric action give indirect support.

Vaginal constriction can be avoided by widely freeing the fascia from the deep surface of the vaginal mucous membrane and by placing the sutures carefully and not too far laterally. Only firm reconstitution of the fascia is necessary, not strangulation.

A true appreciation of the value and efficacy of vaginal hysterectomy, or of any operation for that matter, can only be arrived at by a re-examination of the patient one year and more after operation, preferably by an independent observer, not by the original surgeon.

SUMMARY

(1) One thousand consecutive cases of vaginal hysterectomy performed in the Area Department of Obstetrics and Gynaecology at Oxford between 1943–1956 with only 1 death, a mortality rate of 0·1 per cent, have been reviewed and presented.

(2) Nine hundred and forty-four patients were followed up at six weeks. Four hundred

and sixteen have been re-examined at one year and more after operation. The results are presented.

(3) The greatest post-operative complication was urinary infection. There were no fistulae.

(4) Haemorrhage and sepsis did not constitute major problems. Sepsis if present was extraperitoneal.

(5) The use of uterine ligaments and pelvic fascia in the prevention of vault prolapse and recurrent cystocoele, urethrocoele, enterocoele and rectocoele, is discussed.

(6) The commonest indication for the operation was excessive uterine bleeding (not due to carcinoma) associated with prolapse.

(7) Technique of the operation is described.

Acknowledgments

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OF PERIPHERAL NERVE PALSIES IN THE NEWLY BORN

BY

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THE injuries to peripheral nerves most commonly described in connexion with the newly born are those involving the brachial plexus and the facial nerve. Radial palsy is less frequently described. Eight cases have been recorded by Feldman (1957), 3 each by Morgan (1948) and Langen (1930), and 2 by Lightwood (1951). Other isolated examples have been reported by Kehrer (1918, 1934), Abelson and Greengard (1936), Ottow (1932), Smith (1916, 1935), Krafft (1935), and Loyarte and Daquerre (1953). Hanch and Ottsen (1939) found reference to 25 cases in the literature, discovered records of 6 in their hospital archives, and described 2 further examples observed personally. Holt and McIntosh (1953) state to having seen 2 cases of temporary paralysis affecting muscles supplied by the radial nerve and Ellis (1956, p. 82) refers to the rare occurrence of the condition in the newly born. Eight examples of radial palsy have been seen by the present writers in the newly born. It is the purpose of this paper to describe these cases together with instances of palsy which affected the posterior interosseous (3), lateral popliteal (2) and obturator (1) nerves, and which were detected in infants within a few hours of birth. We have been unable to find detailed references to peripheral nerve palsies affecting the lower limbs in the newly born.

CLINICAL FINDINGS

1. Radial Nerve Palsy (6)

Series No. 1. Baby W., female, birth weight, 6 pounds, estimated gestation period, 40 weeks. Presentation, breech. Labour, normal. Delivery—breech extraction with forceps to the aftercoming head. Mother, aged 30 years, first pregnancy.

At birth the infant's general condition was satisfactory but there was a fracture of the middle third of the left humerus. A large haematoma was palpable in the soft tissues surrounding the fracture site. Left wrist drop was observed within a few hours of delivery. A plaster of Paris splint was applied to the left forearm and wrist. On the second day of life Erb's palsy of the other arm was noted. By the time the child left hospital at the age of one month normal function of both arms and hands had fully recovered.

The left radial nerve palsy was related to the humeral fracture and could be attributed to pressure on the nerve by the haematoma. Another source of pressure might have been bony fragments disturbed in the course of manipulation of the arm. A further possibility is that discontinuity of the humerus favoured traction on the nerve.

Series No. 2. Baby L., female, birth weight, 6 pounds 14 ounces, estimated gestation period, 40 weeks. Presentation, vertex. Labour: prolonged second stage, foetal distress. Delivery, mid-forceps extraction. Mother, aged 32 years, first pregnancy.

At birth the infant was slightly asphyxiated. Regular rhythmic respirations were quickly established. Left wrist drop was noted on the first day of life but the baby was able to grip with the fingers of the affected hand when the wrist was supported. Movements of the elbows and shoulders were unrestricted. Localized superficial bruising was present over the antero-lateral aspect of the middle third of the left upper arm. A "cock-up" splint was applied to the affected forearm and wrist and the paralysis disappeared completely during the course of 9 weeks.

The left radial nerve palsy can be attributed to compression of the nerve at the level of the middle of the humeral shaft at which level there was visible evidence of local trauma.

Series No. 3. Baby S., male, birth weight, 7 pounds 9 ounces, estimated gestation period, 40 weeks. Presentation vertex. Delivery by Caesarean section because of foetal distress and contracted maternal pelvis. Mother, aged 31 years, first pregnancy, severe pyelitis antenatally.

At birth the infant was severely asphyxiated. Signs of moderately severe intracranial disturbance were present during the first four days of life. Thereafter general progress was uneventful. Bilateral wrist drop was present at birth (Figs. 1, 2 and 3). There was voluntary extension of the fingers when the wrists were in the dropped position. Movements of the elbows and shoulders were unrestricted. A "cock-up" splint was applied to each forearm and wrist. At birth extensive, severe contusions of the thorax and arms were noted. The bruising of each arm was situated antero-laterally at a level immediately proximal to the lateral humeral condyle. Bruising of the trunk was situated anteriorly at a level immediately distal to the nipples. The contusions of the trunk and arms were in the same horizontal plane. Eventually all the contused areas necrosed, sloughed and showed scar formation. The infant was able to grip with each hand by the age of one month but the bilateral wrist drop did not completely disappear until the age of three and a half months.

The radial nerve palsies in this infant were caused by the pressure exerted by a uterine contraction ring noted at the time of delivery by the obstetrician and considered by him to be at a level corresponding to that of the contusions found on the infant.

Series No. 4. Baby D., male, birth weight, 8 pounds 8 ounces, estimated gestation period, 40 weeks. Presentation, vertex, right occipito-lateral. Labour, low transverse arrest. Delivery: episiotomy, instrumental rotation followed by forceps extraction. Mother, aged 24 years, first pregnancy.

Forty-five minutes after delivery slight bruising was noted on the antero-lateral aspect of the right upper arm at the level of the middle third of the humerus. Eleven hours later right wrist drop was observed (Fig. 4). Movements at the right shoulder and elbow joints were normal. A "cock-up" splint was applied to the right forearm and wrist. The radial nerve palsy had completely disappeared within 14 days of birth although a small haematoma was still palpable at the site of the original contusion.

The radial nerve palsy can be attributed to compression of the nerve in the region of the contusion at the level of the middle of the humeral shaft.

Series No. 5. Baby Mac, male, birth weight, 8 pounds 12 ounces, estimated gestation period, 41 weeks. Presentation, vertex, persistent occipito-posterior. Delivery: instrumental after manual rotation; difficulty experienced in extraction of the shoulders. Mother, aged 41 years, second pregnancy, first live birth.

The infant's general condition at birth was satisfactory. Slight bruising over the middle third of the lateral aspect of the left upper arm associated with left wrist drop was noticed 12 hours after delivery. The movements of the left shoulder and elbow joints were unrestricted. There was a sense of resistance to passive extension of the fingers but not to passive dorsiflexion of the wrist. The palsy disappeared spontaneously and there was complete recovery of function within three and a half weeks of birth. During the same period a small haematoma on the lateral aspect of the left upper arm gradually resolved.

The left radial nerve palsy can be attributed to pressure on the nerve at the site of bruising in the upper arm.

Series No. 6. Baby T., female, birth weight, 6 pounds 10 ounces, estimated gestation period, 43 weeks. Presentation, vertex. Delivery: Caesarean section because of foetal distress. Mother, aged 38 years, first pregnancy.

On the second day of life the baby developed signs of acute abdominal obstruction. Laparotomy was performed and abdominal adhesions were removed. After closure of the abdomen, intravenous saline was given into the saphenous vein. Five hours after operation right wrist drop was observed (Fig. 5). Movements of the right shoulder and elbow were normal. Neither superficial bruising nor a haematoma was present. The wrist drop gradually improved but did not completely recover for 7 weeks. Treatment consisted of the application of a short "cock-up" splint for the wrist.

The infant was restless during the giving of the post-operative transfusion. In order to control the baby a nurse standing behind the infant's head grasped the middle of each of the infant's upper arms until the transfusion was completed. The radial nerve palsy was attributable to the sustained pressure exerted on the affected upper arm. In effect the equivalent of a tourniquet palsy of the radial nerve was caused.

II. Posterior Interosseous Nerve Palsy (3)

Series No. 7. Baby S., male, birth weight, 8 pounds 8 ounces, estimated gestation period, 40 weeks. Presentation, vertex, persistent occipito-posterior position. Labour: prolonged second stage necessitating admission of the mother to hospital as an emergency because of foetal distress. Delivery: instrumental rotation and mid-forceps extraction; liquor heavily stained with meconium. Mother, aged 38 years, first pregnancy.

At birth the infant was severely asphyxiated but regular rhythmic respirations were established within 12 minutes of delivery. Bilateral wrist drop was commented upon at the time of birth and confirmed in the course of detailed physical examination 8 hours later. The condition was more pronounced in the left wrist. Passive dorsiflexion produced a sense of resistance in the left but not in the right wrist. Movements of both shoulder and both elbow joints were unrestricted. There were superficial abrasions over the postero-medial aspects of both forearms immediately proximal to the wrist joints. In the left forearm there was in addition a small contusion deep to the abrasions. The right wrist drop recovered spontaneously in one week. A "cock-up" splint was applied to the left forearm and wrist and the palsy disappeared completely after a period of 4 weeks.

The palsies cannot be explained by pressure from local trauma at the sites of the abrasions. All the branches of the posterior interosseous nerve supplying the extensor muscles of the forearm arise at a higher level than the visible pressure areas. The resistance to passive dorsiflexion in the left wrist suggests a palmar flexion contracture caused most probably by intra-uterine posture.

The spontaneously disappearing flaccid paralysis of the right forearm extensor muscles suggests temporary

physiological nerve block (neurapraxia) of the posterior interosseous nerve. Any contributory local compressive agent would however have had to act at a higher level than the abrasions in the region of the right wrist, and would moreover have had to act without leaving any visible evidence. The absence of resistance to passive dorsiflexion of the right wrist shows that there was no contracture of the flexor aspect of this joint. Another possible explanation of the neurapraxia is that traction on the posterior interosseous nerve resulted from prolonged intra-uterine palmar flexion. This is regarded as the most probable explanation in view of the observations in connexion with the other (left) wrist.

Series No. 8. Baby M., male, birth weight, 8 pounds 7 ounces, estimated gestation period, 40 weeks. Presentation, vertex. Labour: prolonged second stage; no foetal distress. Delivery, instrumental. Mother, aged 34 years, first pregnancy.

The infant was asphyxiated at birth. Bilateral wrist drop was noticed at the time of delivery. The skin surface of each wrist was smooth over the dorsum but on the anterior aspect there were coarse creases which did not completely disappear after passive extension of the wrist. These findings can be related to the position assumed by the baby at birth and for some hours subsequently. Each arm was moderately abducted at the shoulder, the elbow acutely flexed, the forearm externally rotated and the flexed hand inserted into the corresponding axilla. Movements of the elbow and shoulder joints were unimpaired. No contusions or superficial abrasions were detected. A "cock-up" splint was applied to each forearm and wrist. Full function of the left wrist returned in 10 days and of the right wrist in 2 weeks.

The presence of creases on the volar surface of each wrist suggests that the palmar flexion represented a persistence of the intra-uterine position. Nevertheless the ease with which the deformity could be corrected pointed to the absence of a flexion contracture as found in association with a club hand. To produce posterior interosseous nerve weakness, local pressure would have to be applied at the level of the upper third of the forearm in order to affect the muscular branches of the wrist extensors. There was no visible evidence of any such pressure. It is possible, however, that the prolonged palmar flexion may have caused traction on the posterior interosseous nerves to give rise to a mild neurapraxia which quickly recovered.

Series No. 9. Baby T., male, birth weight, 6 pounds 5 ounces, estimated gestation period, 41 weeks. Presentation, vertex. Labour: foetal heart sounds were slow and irregular at the end of the second stage; liquor stained with meconium. Delivery, spontaneous. Mother, aged 38 years, first pregnancy.

The general condition of the infant at birth was satisfactory. Right wrist drop was observed in the course of a detailed examination 4 hours after birth (Fig. 6). Movements of the shoulder and elbow joints of the affected limb were normal and there was voluntary extension of the fingers. No superficial bruises or abrasions were detected. Radiographs showed no evidence of fracture. A "cock-up" splint was applied to the right forearm and wrist. Improvement in the power of extension of the right wrist was evident on the fourth day of life. By the ninth day the infant was able partly to dorsiflex the wrist and to grip with the right hand. Signs of wrist drop were still present when the baby was examined at the age of one month but were no longer detectable at the age of 7 weeks.

Neither the obstetrical history nor the clinical findings suggested that the right radial nerve palsy was the result of local compression of the nerve. Immediately after birth, and for some days subsequently, the upper limbs remained in an unusual position. The arms were slightly abducted at the shoulders, the elbows flexed and the forearms lay across the front of the chest at a high level. Both wrists were palmar flexed, the forearms were in full supination and each palm faced towards the corresponding axilla. Skin creases were prominent on the anterior aspect of each wrist and absent on the dorsal aspect. The findings in this connexion were less striking than in the infant Series No. 8.

In the absence of evidence indicative of any other aetiology it is considered that the palsy affected the posterior interosseous nerve and was related to the intra-uterine position of the arms. The view is held that, as in infants Series Nos. 7 and 8, prolonged acute palmar flexion of the wrist resulted in traction on the posterior interosseous nerve with consequent neurapraxia. This view is not invalidated by the implication of only one posterior interosseous nerve despite the fact that both wrists were acutely palmar-flexed. It is conceivable that a minor left nerve palsy passed unnoticed during the period preceding detailed examination.

III. Radial Nerve Palsy: Undetermined Level (2)

Series No. 10. Baby B., male, birth weight, 8 pounds 3 ounces, estimated gestation period, 40 weeks. Presentation, vertex. Labour: prolonged second stage with foetal distress. Delivery, instrumental. Mother, aged 25 years, first pregnancy.

The infant was severely asphyxiated at birth. Regular rhythmic respirations were established in approximately 15 minutes. Thereafter progress was uninterrupted. Left wrist drop was noted early on the second day (Fig. 7). Movements at the elbow and shoulders were unrestricted. No bruising or abrasions of the limb were discovered. A "cock-up" splint was applied to the left forearm and wrist and the palsy had completely disappeared after a period of 2 months.

Series No. 11. Baby M., female, birth weight, 6 pounds 15 ounces, estimated gestation period, 42/43 weeks. Presentation, vertex. Labour: induced because of hypertension and post-maturity; pitocin drip given, Delivery, spontaneous. Mother, aged 32 years, third pregnancy, first live birth.

There was a moderate degree of asphyxia of the infant at birth. Bilateral wrist drop was noticed 16 hours after delivery (Fig. 8). The right wrist was more severely affected than the left. There was no evidence of superficial or deep bruising. A "cock-up" splint was applied to the

right forearm and wrist. Voluntary extension of the fingers was first seen at the age of 3 days. Weak movements of voluntary extension at the wrist were first noted on the left on the fifth day and on the right on the seventh day of life. Thereafter improvement was uninterrupted and the palsies completely disappeared by the end of the second week.

Neither the obstetrical histories nor the clinical observations on these last two babies (Series Nos. 10 and 11) provide a conclusive explanation of the palsies. It can be said, however, that in each infant the finding of a peripheral nerve lesion, the complete recovery of function and the vertex presentation are arguments against a brachial plexus traction lesion. In the absence of any clear indication of a defined anatomical level of the lesions it is not possible to decide whether the radial or the posterior interosseous nerve(s) was affected in these two babies.

IV. Lateral (External) Popliteal Nerve Palsy (2)

Series No. 12. Baby H., female, birth weight, 6 pounds 8 ounces, estimated gestation period, 40 weeks. Presentation, breech. Labour, spontaneous. Delivery, breech with extended legs. Mother, aged 27 years, first pregnancy.

The infant's general condition at birth was satisfactory. On the second day of life a pronounced left foot drop was noticed (Fig. 9). There was a large vesicle on the dorsum of the left hallux. Power of active dorsiflexion at the left ankle was entirely absent. There was no other muscular weakness and no detectable loss of sensation. A plaster of Paris splint was applied to the left leg and foot in order to maintain the foot in a neutral position. Disappearance of the lateral popliteal nerve palsy was complete within 6 weeks.

Series No. 13. Baby Mc., male, birth weight, 6 pounds 13 ounces, estimated gestation period, 40 weeks. Presentation, breech. Labour, spontaneous. Delivery, extended legs brought down digitally. Mother, aged 30 years, first pregnancy.

At birth the infant showed some distress but not true asphyxia. Eighteen hours after birth a moderate degree of left foot drop associated with slight inversion of the foot was detected. There was no evidence of abrasion or other injury and no other muscle weakness. Commencing spontaneous disappearance of the lateral popliteal nerve palsy was noted on the fifth day of life and was complete by the seventeenth day.

No splintage was used.

These last two infants (Series Nos. 12 and 13) had in common breech presentation with extended legs, spontaneous onset of labour and a post-natal lateral popliteal nerve palsy. They differed in the mode of delivery. Baby H. (Series No. 12) was delivered with the legs still extended whereas Baby Mc. (Series No. 13) was delivered by the breech after the extended legs had been brought down digitally. If it be accepted that there was a common explanation for the peroneal nerve palsies it should be sought in the similar circumstances preceding delivery rather than the differing circumstances of birth. It would seem reasonable to deduce that the extended lower limbs were responsible for the nerve lesions by traction. The vulnerability of the lateral (external) popliteal nerve may be explained by its relative fixation at the level of the neck of the fibula.

V. Obturator Nerve Palsy (1)

Series No. 14. Baby R., female, birth weight, 7 pounds 3 ounces, estimated gestation period, 40 weeks. Presentation, breech. Delivery, by Caesarean section because of maternal toxaemia. Mother, aged 32 years, first pregnancy.

At birth the infant's general condition was satisfactory and rhythmic respirations were established at once. Immediately after delivery it was observed that the right lower limb lay in a position of full external rotation and abduction at the hip with the knee flexed.

When the infant was examined at the age of 18 hours it was noted that during passive flexion of the right hip and knee, the thigh and leg adopted a position of external rotation and that adductor resistance was absent. It was possible to abduct the limb to 90 degrees. There was slight impairment of active extension of the right knee and marked impairment of active internal rotation and adduction of the thigh indicating paralysis of the right obturator nerve (Figs. 10 and 11). In so far as could be estimated there was no impairment of sensation. No evidence of bruising or abrasions was detected. The right lower limb gradually assumed a normal position and normal adductor and internal rotator function became established. Complete disappearance of the right obturator nerve palsy took place over a period of 10 to 14 days.

No splintage was used.

During birth traction of very moderate degree was exerted on the affected limb and this traction was considered by the obstetrician to be a probable cause of the right obturator nerve palsy. The manual traction referred to was applied in order to deliver the right lower limb. Another possibility which cannot be excluded is that the prolonged abnormal intra-uterine posture was a contributory aetiological factor. In favour of this is the observation of those present at the delivery that the position of the affected limb *in utero* resembled that noted after delivery of the baby.

Discussion

Obstetrical Background

Four infants were postmature and 10 were born at term. No premature baby was seen with peripheral nerve limb palsy. This can probably be explained by the relative smallness of the premature baby and by the fact that, although the premature baby is especially prone to birth trauma, the infant's limbs do not often give rise to obstetrical difficulty and are rarely the site of local trauma when delivery is premature. There

FIG. 1

Baby S. (Ser. No. 3): Aged 36 hours. Bilateral Radial Nerve Palsy due to pressure exerted by uterine contraction ring. Note the bruising of the anterior thorax.

FIG 2.

Baby S. (Ser. No. 3): Aged 36 hours. The same baby as in Figure 1. Note the bruising of the left arm. The depression in the right arm corresponds to the site of a contusion.

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FIG. 3

Baby S. (Ser. No. 3): Aged 25 days. The same baby as in Figures 1 and 2. There has been necrosis and sloughing at the site of pressure on the right arm. Healing is now taking place. Similar changes were present at the sites of trauma on the left arm and anterior thorax.

FIG. 4

Baby D. (Ser. No. 4): Aged 5 days. Right Radial Nerve Palsy due to pressure at the level of mid-humeral shaft.

FIG. 5

Baby T. (Ser. No. 6): Aged 4 days. Right Radial Palsy due to local pressure on the upper arm during transfusion operation.

FIG. 6

Baby T. (Ser. No. 9). Right Posterior Interosseous Nerve Palsy due to traction on the nerve secondary to prolonged intra-uterine palmar flexion of the wrist.

FIG. 7

Baby B. (Ser. No. 10). Left Radial Nerve Palsy: undetermined level.

FIG. 8

Baby M. (Ser. No. 11). Bilateral Radial Nerve Palsy: undetermined level.

FIG. 9

Baby H. (Ser. No. 12). Left Lateral (External) Popliteal Nerve Palsy: due to traction on the nerve secondary to prolonged intra-uterine extension of lower limb in breech presentation.

FIG. 10

Baby R. (Ser. No. 14). Right Obturator Nerve Palsy: due to traction on the nerve secondary to prolonged extreme abduction of the limb *in utero*.

FIG. 11

Baby R. (Ser. No. 14). Right Obturator Nerve Palsy: same baby as in Figure 10.

FIG. 15

Baby M. (Ser. No. 15). Aged 48 hours. Bilateral Nerve Palsy with lesions at undetermined levels.

is further evidence of an expected relationship between the obstetrical background and the incidence of peripheral nerve palsy in the predominance of first babies in the present series. All 14 infants were first live births, 11 representing first pregnancies. This is in keeping with the accepted higher risk of injury at birth of the first born child as compared with subsequent siblings.

In not one of the fourteen cases included in the series were labour and delivery entirely normal. There were 4 breech presentations, the legs being extended in 2, forceps being applied to the aftercoming head in a third, and delivery of the fourth being by Caesarean section. Foetal distress associated with prolonged labour or obstetrical complications was a feature of the delivery in 6 instances of vertex presentation. There was no foetal distress in the remaining 4 deliveries in which presentation was by the vertex, but in 3 of these cases labour was characterized by a prolonged second stage and difficult instrumental delivery, and in the fourth case labour followed induction by a pitocin drip. In each of the 14 infants in the series therefore there was something abnormal in the antenatal history or in the circumstances of labour and delivery or in the clinical course shortly after birth.

There was no known infection in any of the 14 babies.

Time of Recognition

Nerve palsy was detected at birth in 4 infants (Series Nos. 3, 7, 8, and 14) and within 24 hours of birth in 9 babies. In the remaining infant (Series No. 6) wrist drop was noted five hours after an emergency surgical operation. No example was encountered of the delayed appearance of radial nerve palsy reported by Morgan (1948) and Smith (1935). It is not considered that the latent period between birth and the recognition of palsy is of any pathological significance. Experience in the present study demonstrated that with increasing awareness of the possibility of peripheral nerve palsy and with earlier *detailed* clinical examination of the baby the period between birth and the detection of palsy was materially reduced.

Aetiology

General

In each of the 14 infants the condition affecting the peripheral nerve was one of neurapraxia as evidenced by ultimate complete recovery. Temporarily disturbed neural function of this kind is attributable to local nerve ischaemia. Impaired vascularity of a nerve is caused by either local compression of the nerve, or traction on the nerve over a fixed point. The mechanism of local compression in adults has been fully discussed by Garland and Moorhouse (1952) with particular reference to the external popliteal nerve.

Perhaps the best-known example of neurapraxia resulting from local compression is tourniquet palsy. Erb's palsy and Klumpke's palsy are recognized examples of the results of severe traction on the nerve roots. Lesser degrees of traction affect the peripheral nerves as distinct from the roots of the nerves. Traction on a limb does not act detrimentally on all the nerves within that limb. That a particular nerve is affected is determined by the anatomical relation of the nerve to a fixed point over which it is stretched.

Peripheral Nerve Palsies Affecting the Upper Limbs

A number of explanations has been advanced to account for the occurrence of radial palsy in the newly born. Abelson and Greengard (1936) suggested that the palsy might be evidence of foetal intoxication due to the administration of barbiturates or quinine to the mother. In the present series none of the mothers had been given prolonged barbiturate or quinine therapy. Elkington (1942) draws attention to the mechanical dangers of intramuscular injection of sulphonamide drugs, and Ford (1944, p. 935) stresses the risk to the radial nerve of any intramuscular injection in the arm. No intramuscular injections were given to any of the babies in the present series before detection of the palsies. Kehrer (1934) described a case of bilateral nerve palsy which he considered was caused by abnormal pressure exerted by the mother's deformed rachitic pelvis. There was no instance of a rachitic pelvis in the mothers of babies in the present study.

Several observers have drawn attention to evidence of pressure in the neighbourhood of the nerve in examples of radial nerve palsy. Pressure grooves were described by Langen (1930), who considered that they might be due to previously absorbed amniotic bands, and by Ottow (1932), who suggested that the grooves were evidence of pressure by the umbilical cord. Kehrer (1934) and Ottow (1932) are agreed in attributing the presence of haematomata to pressure exerted on the affected arm by the mother's sacral promontory and symphysis pubis. The importance of prolonged labour and rigidity of the cervix is stressed by Hanch and Ottsen (1939), who mention also the occurrence of radial nerve palsy secondary to fracture of the humerus. Baby W. (Series No. 1) in the present series is an example of the latter association. The radial nerve is described by Dunham (1955) as the nerve most commonly involved by pressure from forceps during the delivery of premature infants, and by Ford (1944, p. 934) as the nerve most frequently affected in pressure palsies occurring in adults under anaesthesia. Baby T. (Series No. 6) is an instance of peripheral radial nerve palsy in a newly born infant caused by local pressure exerted during an emergency post-operative procedure.

Hanch and Ottsen (1939), Smith (1935) and Morgan (1948) describe examples of bilateral radial palsy caused by uterine contraction rings. Aetiologically these cases resemble Baby S. (Series No. 3) in the present study. In the baby reported by Hanch and Ottsen a band of transverse pressure involved the back and left arm, and in the infant noted by Morgan there were haemorrhages and pressure marks in the same horizontal plane across the thorax and both arms. Morris (1957) gives a graphic description of unilateral right wrist drop due to direct pressure from annular spasm of the uterus. A line of ecchymosis crossed the posterior thorax and right upper arm and the infant's body was notably oedematous on the cephalic side of the line of ecchymosis.

Lightwood (1951) and Feldman (1957) among others have drawn attention to the occasional association of radial palsy with localized sclerema and subcutaneous fat necrosis in the neighbourhood of the supracondylar portion of the radial nerve. It is doubtful if the nerve palsy in these circumstances is the direct result of pressure or is due to nerve involvement secondary to the sclerematous changes. In the present series fat necrosis and sclerema were looked for with particular care but were not found in any baby including the infant (Series No. 3) in whom there was extensive deep sloughing and the babies (Series Nos. 1, 4 and 5) in whom localized haematomata were found.

Smith (1916) and Peterson (1925) recognized that radial nerve palsy can occur without detectable evidence of local pressure from whatever cause. In a later publication Smith (1935) pointed out that "the presence of pressure marks on the skin is not necessary in making a diagnosis of peripheral facial nerve paralysis . . . in a newborn". Absence of any external evidence of local pressure was a feature of the two babies (Series Nos. 10 and 11) in whom the level of radial nerve trauma was undetermined; and of two babies (Series Nos. 8 and 9) with posterior interosseous nerve palsy. In the third example of posterior interosseous nerve palsy (Series No. 7) the existence of superficial bruising was incidental in so far as it possessed no direct or indirect anatomical relationship to the site of nerve damage. The case of Baby T. (Series No. 6) with signs analogous to those of tourniquet palsy is of particular interest. There were no bruises or ecchymosis. Cause and effect were none the less indisputable. The case was one of radial nerve palsy certainly due to pressure exerted at the level of the middle of the humeral shaft but without evidence of superficial trauma. This does not, however, warrant acceptance of the view that radial nerve palsies in the newly born are invariably to be ascribed to *local* pressure effects.

Browne (1951) attaches importance to abnormal pressure exerted on the foetus before birth as a mechanical cause of certain errors of development. He refers to infants affected in this way as "compression babies". Ecchymoses, contusions and haematomata are not characteristic of antenatal compression. Their presence is in keeping with trauma sustained after the onset of labour.

Ellis (1956, p. 114) suggests that oligamnios may be a contributory or aggravating factor

where intra-uterine compression gives rise to foetal deformities. In the present series oligamnios was not recorded in connexion with the delivery of any, and postmaturity was a feature of 2 babies (excluding Baby Series No. 6). Obstetrical opinions differ concerning the finding of absolute or relative hydramnios in association with postmaturity. The theory that by giving rise to excessive pressure on the foetus *in utero* postmaturity favours the development of deformities and nerve palsies is attractive. It is possible that this may have been a factor in the posterior interosseous nerve palsy found in Baby Series No. 9. In the series as a whole, however, postmaturity was not a contributory causal factor of peripheral nerve palsy.

Among babies with wrist drop in the present series the 3 with posterior interosseous nerve palsy (Series Nos. 7, 8 and 9) could be regarded as possible examples of "compression babies". Abnormal palmar flexion was present in all 3 at birth. It is considered that the prolonged intra-uterine palmar flexion was responsible for traction on the posterior interosseous nerve over the relatively fixed point at the origin of the nerve in the supinator muscle (Fig. 12).

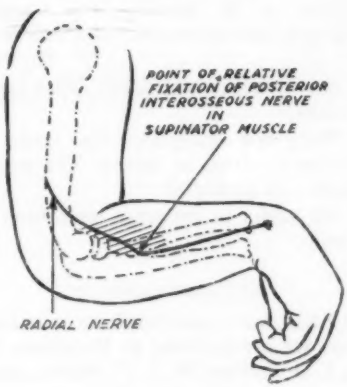

FIG. 12

Diagram to show the course of the radial and posterior interosseous nerves and the suggested relative fixed point on the outer aspect of the elbow when traction on the posterior interosseous nerve is induced by full palmar flexion of the wrist.

Peripheral Nerve Palsies Affecting the Lower Limb

Discussing peripheral nerve injuries in the newborn, Von Reuss (1920) and Brennemann (1956) comment upon the extreme rarity with which paralysis of the lower extremities is found. Both these authorities consider that damage results from stretching of the lumbar plexus by excessive traction on the legs during breech delivery. Von Reuss (1920) quotes Bruns *et al.* (1912) as holding the view that paralysis affecting the lower limbs probably occurs frequently but disappears rapidly.

Paralysis of the lower extremities was a feature of 2 cases (Series Nos. 12 and 13) delivered by the breech in the present series. In both instances the legs were extended. It is to be emphasized, however, that in each baby impairment of nerve function was limited to the lateral (external) popliteal nerve. The isolated involvement of this nerve cannot be attributed to traction on the lumbar plexus. Nevertheless it can be explained by the traction exerted on the whole sciatic nerve because of the prolonged extension *in utero* of the lower limbs. Although insufficient to produce paralysis of the relatively free internal portion of the popliteal nerve, the traction exerted a selective effect on the lateral popliteal nerve. This selective effect is to be explained by the relative fixation of the nerve at the neck of the fibula. The consequent local ischaemia accounts for the paralysis distal to the neck of the fibula (Fig. 13).

The third baby was an instance of obturator nerve palsy (Baby Series No. 14). *In utero* the affected limb had been maintained for a prolonged period in a position of extreme flexion, abduction and external rotation at the hip. After leaving the obturator canal the normal course of the obturator nerve is straight into the thigh. The nerve ends in muscular branches above the knee and an articular branch to the knee joint. With the extreme flexion and abduction at the hip in this infant the obturator nerve was "hooked" around the pubic ramus. As a result the nerve was stretched between two fixed points, viz., the pubic ramus and the knee joint. The local ischaemia of the nerve at the proximal point of fixation (the pubic ramus) produced the paralysis distal to that level

FIG. 13

Diagram to show the course of the sciatic nerve and the suggested relative fixed point at the neck of the fibula when traction on the external popliteal nerve is induced by full extension of the lower limb.

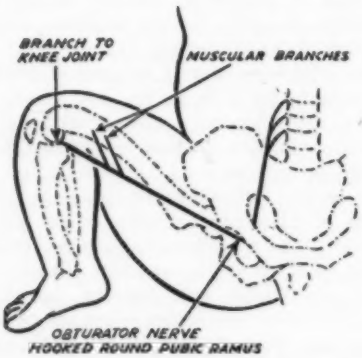

FIG 14

Diagram to show the course of the obturator nerve and the suggested relative fixed point on the pubic ramus when traction on the nerve is induced by full flexion, abduction and external rotation of the lower limb.

(Fig. 14). Aetiologically this is in accordance with the views outlined with regard to the examples of lateral popliteal and posterior interosseous nerve palsies.

PROGNOSIS

The peripheral nerve palsy in each of the 14 newly born babies recovered completely. By reason of their aetiology the lesions are to be regarded as examples of neurapraxias. Implied in the conception of neurapraxia is ultimate functional recovery.

SUMMARY

(1) Fourteen examples of peripheral nerve palsy in newly born infants are described.

(2) The nerves affected were radial (8), posterior interosseous (3), lateral popliteal (2) and obturator (1).

(3) Nerve palsy was detected at birth in 4 and within 24 hours of birth in 9 infants. In the remaining baby palsy was noted 5 hours after post-operative transfusion.

(4) Each palsy recovered completely and was an example of neurapraxia.

(5) Each palsy is attributed to local ischaemia of the nerve produced either by compression of the nerve, or by traction with consequent stretching of the nerve over a relatively fixed point.

(6) Each instance of traction lesion occurred antenatally.

(7) With one exception the compression lesions were related to labour. The exception was iatric and postnatal.

(8) All babies in the series were born at or after term.

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Addendum

Since submission of this paper a further example of pronounced bilateral radial nerve palsy has been seen. The following are particulars.

Series No. 15. Baby M., female, birth weight 8 pounds 8 ounces, estimated gestation period—41 weeks. Presentation—vertex. Labour—persistent occipito-posterior. Delivery—by Caesarean section on account of presentation of cord. Mother—aged 23 years: second pregnancy.

The infant was distressed at birth. Regular rhythmic respirations were established in approximately 7 minutes. The position of the hands and arms *in utero* was not seen. Bilateral wrist drop was noted two hours after birth. Movements at the elbows and shoulders were unrestricted. No bruising or abrasions were detected. "Cock-up" splints were applied to the forearms and wrists and the palsies completely disappeared 4 weeks after birth. In the absence of a defined level of the lesions it is not possible to state whether the radial or the posterior interosseous nerves were affected (Fig. 15).

HYDATIDIFORM MOLE AND ITS COMPLICATIONS

BY

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INTRODUCTION

HYDATIDIFORM mole has been recognized as an entity probably since the time of Hippocrates. While it is not a common complication of pregnancy among the white races it is seen often enough in hospital practice to warrant constant vigilance. Brews (1939), Novak (1948) and Hertig (1950) consider it occurs in about 1 in 1,500 to 1 in 2,500 pregnancies. For some unknown reason it is much more frequent in the Philippines (Acosta-Sison, 1949) and in Hong Kong (King, 1956). These figures apply only to the typical total hydatidiform mole. Minor degrees of hydatidiform degeneration of the chorionic villi, recognizable only on magnification, are often found in aborted ova. Opinions differ as to whether these changes are simply degenerative (Novak, 1952) or represent an early subclinical phase of hydatidiform mole (Mall and Meyer, 1921; Hertig and Edmonds, 1940; Brews and Bender, 1955).

In King George V Memorial Hospital, Sydney, from July, 1943 to June, 1956, 64 hydatidiform moles, including non-booked cases, were seen in 52,452 pregnancies, an incidence of 1 in 820. This paper is based on an analysis of the case records and pathological material of these 64 consecutive cases. The series includes 5 cases of invasive mole, of which 1 was complicated by choriocarcinoma. Only cases where the total hydatidiform mole was obvious macroscopically are included in the series.

Pathological Definition

Benign hydatidiform mole, invasive mole (chorioadenoma destruens, malignant mole, penetrating mole) and choriocarcinoma (chorionepithelioma) will be briefly defined. It will be seen that one of the chief criteria on which the diagnosis of invasive mole and choriocarcinoma depends, that is the type, amount and depth of trophoblastic penetration into the uterine wall, cannot be determined from examination of the curettage material. Even after hysterectomy, mistakes in diagnosis are still made. The main reason for this confusion is the fact that even normal trophoblast, as a result of its invasive properties, exhibits some of the characteristics associated with malignancy.

In typical benign hydatidiform mole the activity of the trophoblast covering the villi may be only slight or of quite marked degree but there is no penetration of the myometrium by the villi. However, as in normal pregnancy, at the placental site there may be invasion of trophoblastic cells (without villi) through the decidua into the myometrium. After pregnancy or the expulsion of a benign hydatidiform mole these cells occasionally persist and become associated with some inflammatory reaction. This condition is known as syncytial endometritis (Fig. 1). It is now recognized as a benign condition and has frequently been mistaken for invasive mole and choriocarcinoma both on examination of curettage material and, by those not familiar with the associated myometrial infiltration, after hysterectomy (Hertig, 1950; Novak, 1952). In this condition, however, the infiltration is chiefly syncytial and unlike choriocarcinoma the cells infiltrate singly or in narrow columns and not in masses and there is no destruction of tissue.

The invasive hydatidiform mole (Figs. 2, 3, 4, 5) is characterized by the presence of one or more villi, with associated trophoblast, in the

myometrium. This molar penetration may take place before or after the expulsion of a hydatidiform mole and can usually be determined only after hysterectomy. With such a broad definition, adopted by Hertig and Mansell (1956) and others, it is advisable to differentiate this group further. King (1956) describes three types of invasive mole which, from the experience in this hospital, seems to be a most practical subdivision. He defines a "simple invasive mole" as one in which the only difference from an ordinary benign mole is the presence of slight to moderate myometrial invasion by villi. The second type, "invasive mole with signs of regression" follows the first type and shows obvious regression of the molar elements. It is likely that some of these cases escape diagnosis, failing to produce any indication for hysterectomy. The third type, "invasive mole with signs of progression", is the classical case which, in its severest form, may show extension to the peritoneal surface, the parametrium or the vaginal vault and is usually associated with much trophoblastic proliferation. It is this last type which corresponds to the more restricted definition of invasive mole given by Novak and Seah (1954a, b).

The frankly malignant choriocarcinoma (Fig. 6) is most easily distinguished microscopically from invasive mole by the absence of chorionic villi. In the former condition the trophoblastic proliferation of both syncytial and Langhans' elements is so excessive that the original villous pattern is completely lost. Novak and Seah (1954a) state however: "theoretically there appears to be no reason why one might not occasionally find vestiges of the villi from whose trophoblastic covering the tumour has arisen" but in their review of findings from the 74 cases of choriocarcinoma in the Mathieu Registry they found villi present in only 1 case. The trophoblastic cells usually show some degree of anaplastic activity. Hertig (1950) considers this is of great importance, but one must agree with Novak (1952) and Hunt, Dockerty and Randall (1953) of the Mayo Clinic who say that judging from the histological appearance of the trophoblastic cells it would be impossible to distinguish invasive mole from choriocarcinoma in a region where there are no villi.

Benign and Malignant Metastases

It is known that normal living trophoblast may also invade the uterine blood vessels and be carried to distant organs and it is probable that such physiological emboli of trophoblast, with or without chorionic villi, occur frequently, if not in all cases of normal pregnancy. This was first suggested more than 50 years ago by Schmorl (1904) who found syncytium in the pulmonary capillaries of 80 per cent of 158 autopsies of women dying during pregnancy and in the puerperium. It is also likely that a similar blood stream transportation occurs in many cases of benign and invasive hydatidiform mole. Thus Hughes (1930) discovered masses of syncytial cells on examination of the lungs of a woman who died with a hydatidiform mole *in situ*; and Miller (1923) found actual chorionic villi in the lungs of a patient with invasive mole. There is also evidence that trophoblastic emboli, if extensive enough, may actually cause maternal death in normal pregnancy (Marcuse, 1954) and in hydatidiform mole (Trotter and Tieche, 1956).

Although these trophoblastic emboli may occur frequently, it is exceptional for actual clinical symptoms to be produced in normal pregnancy and uncommon in cases of hydatidiform mole. When there is such evidence, whether clinical or radiological, the term "benign metastasis", although not altogether satisfactory, may be used. The symptoms are probably due to one of two causes: an embolic phenomenon as mentioned above, similar to pulmonary infarction and occurring while the pregnancy or mole is still *in situ* or, secondly, an actual proliferation of the transported trophoblast which, unlike a true malignant metastasis, is presumably in most cases later destroyed by some unknown lytic process. The commonest sites for metastases are the lungs and vagina.

Pulmonary Metastases. In the present series of 64 hydatidiform moles there was evidence of benign trophoblastic pulmonary metastases in 2 cases of benign mole and 3 cases of invasive mole. In the 2 cases of benign mole (Cases 17 and 59) the diagnosis of pulmonary metastases was made purely on clinical grounds. In both patients haemoptysis was the first sign that the pregnancy was abnormal and in both it recurred

before the abortion of a perfectly benign hydatidiform mole. Physical examination, repeated X-rays, examination for tubercle bacilli and full haematological studies proved negative. There was no history of a previous haemoptysis nor has there been a recurrence since. Both patients are well, one 8 years, the other 18 months, later. In such cases, in which no radiological lesion is seen, there is, of course, no absolute proof of the presence of these metastases. However, as the histories are so typical of other reported cases and there was no other obvious cause for the haemoptysis, it is highly probable the diagnosis is correct. Since the completion of this series there has been one further case in this hospital. One similar case was described by Brews (1939) in his series of 100 moles, another was mentioned by Novak (1950), while Park and Lees (1950) collected 8 cases from the literature reported as choriocarcinoma in which regression of pulmonary metastases was claimed on the clinical grounds of appearance and cessation of haemoptysis. It is likely that some, if not all, of these cases were benign or invasive hydatidiform moles with benign pulmonary metastases.

Radiologically demonstrable pulmonary metastases which subsequently underwent regression were present in 2 cases of invasive mole in this series. These case histories (Nos. 47 and 52) are described fully later. In one, the metastases appeared prior to hysterectomy and had regressed in 3 months. In the other, they followed hysterectomy and had disappeared 6 months later. Other instances of regression of radiologically proved pulmonary metastases in cases of invasive mole have been reported in the literature by Park and Lees (1950), Savage (1951), Hunt *et al.* (1953) and Novak and Seah (1954b). A similar resolution of radiological metastases has been described in a case of syncytial endometritis (Kistner, 1952) and in association with benign hydatidiform mole (Novak and Seah, 1954b).

It is probable that on occasions regression of these primarily benign pulmonary metastases does not occur but choriocarcinoma later develops. The fifth case in this series with pulmonary metastases, which is described in full later, is suggestive of this occurrence. This patient, Case 38, had a total hysterectomy for a large invasive mole. In the preceding week she had had two small haemoptyses, suggesting the possibility of benign pulmonary metastases. Radiological examination of the chest at this stage proved negative. She remained well for 6 months but then developed a troublesome cough with blood-stained sputum. X-ray showed multiple metastatic deposits in the lungs and she died shortly after. Autopsy proved the presence of these malignant metastases and showed the operation site to be clear. An alternative explanation for the development of metastatic choriocarcinoma in the lungs in this case is that choriocarcinoma had already developed in some part of the uterine wall before hysterectomy. This hardly seems possible, however, as the whole tumour was formed by a mass of vesicles.

Practically, in any particular case, it is of course impossible to determine at the time of diagnosis, and for some time after, whether these radiologically demonstrable pulmonary metastases, occurring in association with invasive mole or even benign mole, are merely benign or whether they are truly malignant—a most important factor in the assessment of prognosis. However it is probable that, in the vast majority of these cases in which villi are present in the uterine lesion, the course is benign and it may be assumed that the pulmonary metastases are benign and, unlike those associated with choriocarcinoma, can be expected to regress.

Malignant metastases occurring in association with choriocarcinoma are much more frequent than the benign metastases encountered in benign and invasive mole, and occur in from 55 per cent (Novak and Seah, 1954a) to 80 per cent of cases (Hertig, 1950). Once these metastases have occurred the outcome is nearly always fatal, although there seem to be a few authentic cases in which metastatic growths regressed spontaneously after the primary tumour was removed (Lackner and Leventhal, 1932; King, 1956). Mazer and Edeiken (1933) and Johnson (1951) described similar cases but with short follow-up. However, regression of these lung metastases is so rare that in a proved case of choriocarcinoma it should not necessarily be regarded as a favourable sign. Thus

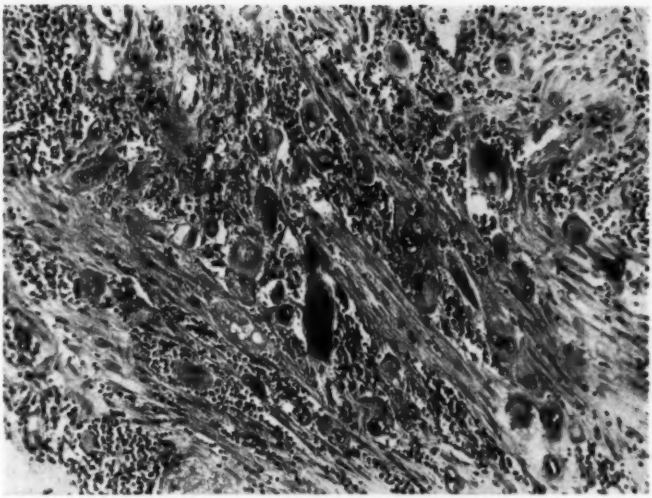

FIG. 1

Syncytial endometritis. Trophoblastic and chronic inflammatory cells infiltrating between uterine muscle fibres. No destruction of tissue. This is a benign condition sometimes mistaken for choriocarcinoma. It may occur after hydatidiform mole, abortion or normal pregnancy. H. & E. ×52.

FIG. 2

Invasive mole of the regressive type (Case 27). Degenerating chorionic villus in the uterine muscle. H. & E. ×52.

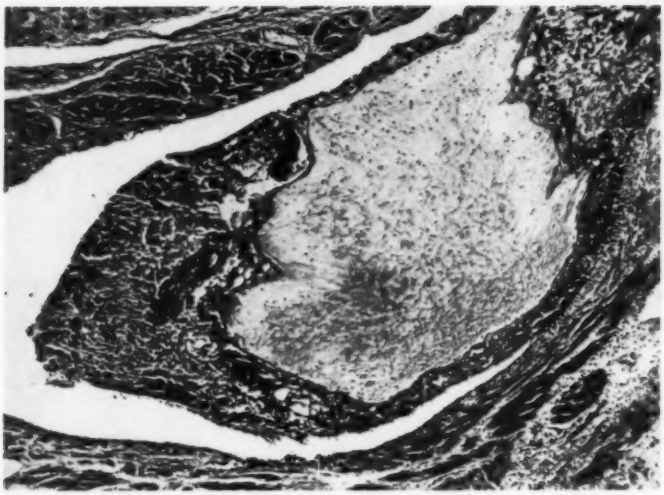

FIG. 3

Invasive mole of the progressive type (Case 47). Chorionic villus in outer half of myometrium. H. & E. ×52.

FIG. 4

Invasive mole of the progressive type (Case 38). Chorionic villi in outer half of myometrium. Patient later died of metastatic choriocarcinoma. H. & E. ×75.

FIG. 5

Invasive mole of the progressive type with villi in the broad ligament (Case 52). (*a*) Outer edge of uterine muscle. (*b*) Chorionic villi in broad ligament. (*c*) Blood clot. H. & E. ×6.

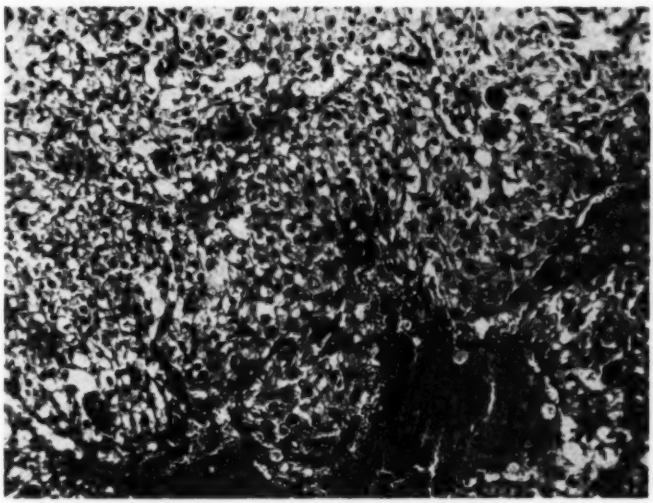

FIG. 6

Choriocarcinoma. Metastasis in lung (Case 38). H. & E. ×105.

M.C.

FIG. 7
Invasive hydatidiform mole (Case 47). Operation specimen.

FIG. 8
Invasive hydatidiform mole (Case 38). Operation specimen. Patient later died of metastatic choriocarcinoma.

Peel, Dawson and Mather (1955) described a case and mentioned another (Peightal, 1934) in which shrinkage and even disappearance of lung shadows occurred yet the patient later died from metastases. Autopsy was performed in the latter case and growth was found to be still present in the lungs. Peel suggests this shrinkage was probably due to the absorption of haemorrhage which surrounded the metastatic cells.

Vaginal Metastases. There were no vaginal metastases in this series but as with pulmonary metastases they may be benign or malignant. The vagina is the second most common site of metastasis in cases of choriocarcinoma, the incidence varying from 16 per cent (Novak and Seah, 1954a) to 50 per cent (Hertig, 1950). Instances of regression of these metastases have been reviewed by Park and Lees (1950) but it is probable that many of them were in fact benign. Vaginal nodules occurring in benign and invasive moles have been discussed by Haines (1955) who says they may even occur in normal pregnancy. Macroscopically these nodules are indistinguishable from those occurring in choriocarcinoma, but histologically he distinguishes between benign and malignant types. Haines points out that the growth of the benign nodule is not due to cell proliferation but to haemorrhage resulting from the deported trophoblast which retains its erosive property.

It is likely, as Haines suggests, that this is the explanation of at least some of the cases in which metastases (pulmonary and elsewhere) have disappeared. The remainder, and also those rare cases in which even the primary choriocarcinoma has undergone spontaneous regression (Novak and Koff, 1930; Hertig, 1950), still await satisfactory explanation. Perhaps Novak's (1948) theory may be the answer. He postulates the presence of a maternal antitrophoblastic defence mechanism varying widely in degree, which he believes checks any trophoblastic invasion whether it be uterine or systemic.

Clinical Features

Incidence

Age. In this series the age varies between 15 and 50 years. Of the 64 patients, 9 were in their teens, 36 were between 20 and 29, 15 between 30 and 39, and only 4 were over the age of 40.

Parity. Forty-eight per cent were primigravidae. The average fertility was 2 full-term pregnancies. One patient had hydatidiform moles in successive pregnancies.

Maturity. All patients at the time of abortion or evacuation of the mole had had a period of amenorrhoea. In 22 patients this varied from 8 to 12 weeks, in another 25 patients from 13 to 19 weeks. In the other 17 cases, the amenorrhoea was prolonged beyond 20 weeks, the maximum time being 26 weeks. It is probable that the vast majority of hydatidiform moles, if undiagnosed, will abort spontaneously by the 26th week.

Symptoms and Signs

Vaginal bleeding following a period of amenorrhoea was almost always the first sign. It occurred in all but one case. Often it was only slight. On other occasions excessive haemorrhage occurred, mostly during or after expulsion of the mole, but occasionally before the onset of contractions. These latter haemorrhages may be the result of penetration of large sinuses or may possibly be caused by a hypofibrinogenaemia (Scott, 1955). The bleeding commenced usually in the second and third months, but twice it did not begin until the 22nd week. In 40 cases (62 per cent) the patient had been bleeding vaginally for over 4 weeks before the mole was spontaneously expelled or surgically removed.

Vomiting. Hyperemesis is apparently more frequent in hydatidiform mole than in normal pregnancy. In this series vomiting was considered severe in 19 cases (30 per cent) and occurred in lesser degree in many others.

Hypertension and Albuminuria. Pre-eclampsia occurred in 5 patients (8 per cent). The criteria for this diagnosis were a blood pressure greater than 140/90 and the presence of albumin in a catheter specimen of urine. In 2 other cases albuminuria was noted. The pre-eclampsia may be most severe and 2 cases were considered fulminating types. The blood pressure in one reached a level of 180/110 at the 16th week, in the other 220/140 at the 22nd week. In both the urine was almost solid with albumin by the boiling test. The incidence of toxaemia has been placed at between 10 per cent and 40 per cent

by various authors but it obviously depends upon the criteria used. No patient in the present series developed eclampsia but this is a possible complication (Chesley, Cosgrove and Preece, 1946).

Size of Uterus. In this series the size of the uterus, in the 51 cases from which no molar tissue had escaped on admission, is set out in Table I.

TABLE I
Size of Uterus

	Per cent
Larger than duration of pregnancy suggested	29–57
Same size as duration of pregnancy suggested	14–27
Smaller than duration of pregnancy suggested	8–16

The findings of other authorities in regard to this matter differ. Brews (1939) found the uterus to be bigger than expected in 72 per cent of cases; King (1956) in 67 per cent; Mathieu (1937) in 50 per cent and Chesley *et al.* (1946) in only 33 per cent. All 4 authors described cases in which the uterus was smaller than the expected size. The histology in such cases in this series usually showed the presence of degenerate and necrotic hydropic villi.

Ovarian Cysts. These were noted in 17 cases (27 per cent) and were usually bilateral. It has been generally accepted that theca lutein cysts occur in about 50 per cent of cases (Das, 1938; Mathieu, 1937). Hertig (1950) says they reach significant size in only 10 per cent. Novak (1952) questions these statistics and believes that if cases were examined daily a greater or lesser degree of cystic change would be noted in all cases.

Other. Anaemia due to blood loss was common. Haemoptysis was the presenting symptom in 2 of the cases. It recurred on both occasions but was unassociated with any radiographic changes in the lungs. Its cause must remain obscure, but as suggested earlier it was probably due to an embolus of trophoblast from the mole resulting in a benign pulmonary metastasis. Passage of vesicles was only noted in this series after labour had begun. Foetal movements were always absent and foetal heart sounds never heard. Pain, apart from its association with abortion of the mole, was not a characteristic symptom. Spontaneous expulsion of the mole occurred in 28 cases (44 per cent) and may be the first indication of its presence.

Investigations

X-ray for foetal parts was performed in many cases and each time the report was "no foetal parts seen". When no foetal parts are seen on examination of a uterus larger than the size expected of an 18-weeks pregnancy, a hydatidiform mole may be suspected. However, it must be remembered that this excessive uterine size may be caused by hydramnios or a twin pregnancy, in which cases the foetus or foetuses are not yet of sufficient maturity to be visualized by the radiograph.

Hormone Assays. Quantitative hormone assays have proved of value as an accessory aid to diagnosis. The Friedman test has been used in this hospital until recently but has now been replaced by the Galli-Mainini test. The results obtained in the 22 cases in which the test was performed before the expulsion of the mole are shown in Table II.

TABLE II
Results of Friedman Test in 22 Cases

	Cases
Positive 1 in 200	15
Positive 1 in 100	4
Positive with undiluted urine (negative 1 in 50)	2
Negative	1

Certain limitations to the quantitative test in diagnosis were evident in this series. In 1 case the test was negative. This was probably due to the necrosis of the mole as the uterus was small and the villi degenerate. Hobson (1955) mentions 3 other cases with repeated negative biological tests. In 2 other cases in the present series the test was positive with undiluted urine but negative in urine diluted 1 in 50 and so therefore useless in differentiating from normal pregnancy. In normal pregnancy, and particularly in multiple pregnancy, there may be a very high hormone peak lasting from 2 to 3 weeks at

about the 10th week of pregnancy (Boycott and Smiles, 1939). At this time the tests may be positive with urine in dilutions of 1 in 200. Hobson (1955) had 2 cases of twin pregnancy with tests positive 1 in 100 as late as the 17th and 20th weeks of pregnancy. Thus, although hydatidiform mole tends to show higher levels of chorionic gonadotrophin in the urine than in normal pregnancy, in any single case the biological test *per se* is not diagnostic.

Treatment

Treatment after Spontaneous Expulsion

Thirty-two (50 per cent) of the hydatidiform moles in this series were spontaneously expelled. Twenty-eight of these cases were then curetted, most often within 24 hours of expulsion and in only 5 cases curettage failed to reveal residual molar tissue. This fact emphasizes the importance of routine curettage following expulsion.

Vaginal Evacuation

In the other 32 cases the mole was surgically evacuated. The vaginal method, which is the simplest, has proved safe and effective and was used in all but 3 cases in this series. In general the following treatment was adopted. If the diagnosis was uncertain the patient was treated conservatively but once the diagnosis was definite the uterus was emptied as soon as possible. This was occasionally achieved by a medical induction using pitocin, either in intermittent dosage or by an intravenous drip. If 2 inductions failed operative removal was performed.

Table III

Immediate Treatment in 64 Cases

Medical:	
After spontaneous evacuation	4
Surgical:	
(*a*) Vaginal:	
Dilatation and curettage	22
Surgical induction and curettage ..	7
Incomplete spontaneous evacuation then curettage	28
(*b*) Abdominal:	
Abdominal hysterotomy	2
Abdominal hysterectomy	1

The disadvantages of the vaginal method of treatment can usually be overcome. Incomplete evacuation of the mole is said to be a disadvantage and recently therefore, in this hospital, a re-curette has been performed routinely 7 to 10 days after the original curettage to ensure that no accessible chorionic tissue remains in the uterus. It is surprising that in only 2 of these 17 cases has residual molar tissue been found. The re-curette has however a further advantage as it allows more accurate assessment of the position in those cases which require a later curette for continued bleeding or other causes. Haemorrhage can usually be controlled by intravenous ergometrine (0·5 mg.), an intravenous pitocin drip throughout the operation, and bimanual compression. In this series a blood transfusion was given in 20 cases (31 per cent), but in many the haemorrhage at the time of operation was not the indication as considerable bleeding had taken place before. There was no case of perforation of the uterus. This risk is greatly reduced by delaying curettage until the end of the operation and using the large blunt curette. Laceration of the cervix may be avoided by the introduction of laminaria tents if any difficulty in dilatation of the cervix is encountered. Curettage is then delayed for about 24 hours. The antibiotics have modified the incidence of post-operative infection. A moderate pyrexia (temperature persisting over 100° F. for at least 2 readings) occurred in 7 cases (11 per cent). Only 1 patient had a severe infection.

Abdominal Hysterotomy

This operation is rarely necessary and was performed only twice in this series. These cases well demonstrate the special indications. In Case No. 14 there was excessive haemorrhage with a very large uterus and a long uneffaced and almost closed cervix. This patient required three litres of blood. The risk of trauma and further haemorrhage in attempting to remove the great mass of molar tissue through a slightly dilated cervix were considered too great. The second indication was a severe fulminating toxaemia in a patient (Case No. 27, described later) with a grossly enlarged uterus and an unfavourable cervix.

Abdominal Hysterectomy

Total hysterectomy was only performed on 1 patient in this series (Case No. 36), a primigravida aged 50 with associated fibromyomata uteri. This is the best treatment in women approaching the end of the childbearing period and who have the required number of children. By this means the risk of choriocarcinoma developing is eliminated.

Treatment of Ovarian Cysts

As a rule the bilateral lutein cysts require no treatment as they involute spontaneously once the mole is evacuated. On occasions, however, a cyst may undergo torsion and must be removed. This event occurred twice in this series.

Complications

The primary mortality in cases of hydatidiform mole is negligible. In this series of 64 cases there were no deaths.

The chief complications are, of course, the development of an invasive mole, or more seriously, a choriocarcinoma. These conditions as a rule develop some time after the expulsion of the hydatidiform mole. Hertig and Mansell (1956) say they have never heard of a case of choriocarcinoma diagnosed from curettings obtained at the time or soon after removal of the mole although they consider this is theoretically possible. On the other hand it is known that some hydatidiform moles are already invasive (e.g., Case 52 in this series) at the time of their spontaneous expulsion or evacuation.

Invasive Mole. In this series there were 5 invasive moles in 64 cases (8 per cent). In the series of Hunt *et al.* (1953) it occurred in 3 of 41 cases (7 per cent). Park and Lees (1950), Corscaden (1951) and others believe it constitutes about 5 per cent of hydatidiform moles.

The malignancy of these tumours is classically one only of local invasiveness. In 2 cases in this series (Case histories 32 and 52) there was extension of the mole into the broad ligament. This may be direct from penetration of the uterus or a local metastasis. Distant metastases are said to occur only rarely (Novak, 1950; Hertig, 1950). It is interesting that 3 (Case histories 47, 52 and 38) of the 5 cases in this series developed pulmonary metastases and although the number of cases is small, it is suggestive that the incidence of metastases might be higher than is generally realized. Their significance and the tendency towards spontaneous regression in some of them has already been discussed earlier in this paper.

Metastatic choriocarcinoma may rarely develop after hysterectomy for invasive mole (Case history No. 38). Presumably in these cases choriocarcinoma has either developed in deported trophoblast or was actually present in the uterus before hysterectomy in association with the invasive mole. The extreme rarity of this association, choriocarcinoma in the presence of villi, has already been mentioned (Novak and Seah, 1954a). Choriocarcinoma may also develop if the uterus is not removed but again this is rare. Thus in some cases an invasive mole may be an intermediate stage in the development of choriocarcinoma, but this is, of course, not necessarily the case.

In general, invasive mole has a good prognosis after hysterectomy. Of the 5 invasive moles in this series, one died of metastatic choriocarcinoma, while the other 4 which will now be described are alive and well after follow-up periods varying from 2 to 5 years. Most deaths reported in the literature have resulted from haemorrhage, sepsis, and perforation of the uterus with fatal haemorrhage; causes which are largely preventable today. Only rarely is death caused by metastatic choriocarcinoma or the metastases associated with invasive mole in which the presence of villi on histological examination does not permit the diagnosis of choriocarcinoma. Thus Novak and Seah (1954b) have followed up 26 cases of invasive mole; 6 were dead but only 1 death could be attributed to metastatic growth. Seventeen of 47 cases in Park and Lees (1950) series proved fatal but in only 2 or perhaps 3 did the mole kill by metastatic spread.

Case History No. 27

Clinical Notes

This patient was a primigravida aged 20 years who was admitted to hospital on the 27th March, 1951, with a provisional diagnosis of hydatidiform mole. Her blood

pressure was then 145/90. The blood pressure continued to rise despite heavy sedation and reached 180/110, at which time the urine showed half of a test tube of albumin by the boiling test. In view of the fulminating toxaemia and an unfavourable cervix, abdominal hysterotomy was performed under local anaesthesia (Prof. Bruce Mayes) and a hydatidiform mole was evacuated. The histological report (Dr. Mary Heseltine) was as follows: "The chorionic villi are atrophic and avascular. There is relatively little activity of the trophoblast and according to Hertig's classification the mole would fall into Group II." On the 3rd May, 6 weeks later, bleeding began again *per vaginam*. Examination revealed a hard nodule about 2·5 cm. in diameter at the lower end of the hysterotomy scar and a bulky uterus. The Friedman test was positive in a dilution of 1 in 200. On the 11th May curettage was performed and some irregular fragments of tissue were obtained in which no evidence of vesicle formation could be found. The histological report (Dr. Mary Heseltine) read: "In the original sections examined, the tissue consisted of regenerating endometrium with some fragments of tissue in which the trophoblast resembled frank choriocarcinoma. However, further sections showed in addition to these areas, isolated vesicles. Because of this, the classification of this tissue should be hydatidiform mole, but it must be remarked that there is extraordinary activity of the trophoblast which accounts for the original opinion that this was a choriocarcinoma. Large plaques of Langhan's cells merge with plaques of very active syncytial cells."

Operation (Mr. Clement Chapman) 18th May, 1951.

Total hysterectomy and right salpingo-oöphorectomy was performed. The left tube and ovary were conserved. The nodule in the abdominal scar was excised.

Pathology (Dr. Mary Heseltine). Operation specimen

Macroscopic. The uterus measures 8·75 cm. in length, 5 cm. in width and 4 cm. in the antero-posterior direction. On the anterior wall is a firm mass of what appears to be scar tissue. On incising the uterus on the posterior aspect a small pink nodule is found measuring 2·5 cm. in width, high in the fundus and situated beneath the endometrial surface. The ovary is not enlarged and on incision shows no special features. Portion of the peritoneum and rectus muscle is submitted separately and measures 3×2·5 cm.

Microscopic. The section taken from the firm mass of tissue in the anterior wall of the uterus consists largely of scar tissue in which numerous inflammatory cells are present. However, the section taken from the posterior wall shows, just beneath the endometrium, which is quite atypical, a solid plaque of cells resembling trophoblast. Further examination of the tissue shows in this particular area in the posterior wall several degenerate looking vesicles. In view of these vesicles a diagnosis of invasive mole seems the correct one. Some cystic follicles and numerous primordial follicles are present in the ovary. The section taken from the rectus muscle shows very marked inflammatory changes.

Follow Up

On the 4th July, 1951, the Friedman test was negative. The patient has been seen at regular intervals since, and is now well over 5 years after the operation.

CASE HISTORY NO. 32

Clinical Notes

This patient was a primigravida aged 24. Spontaneous expulsion of a typical hydatidiform mole occurred on the 20th December, 1951, and residual molar tissue was removed at curettage the next day. The sections, reported on by Dr. Mary Heseltine, showed "typical hydatidiform mole with large hydropic avascular villi. The trophoblast covering a number of the villi shows a moderate degree of activity and the mole is classified as Group IV (Hertig)." When seen 5 weeks later the patient had had only a slight amount of vaginal bleeding since discharge from hospital. The Friedman reaction was still positive in dilution and examination revealed the uterus to be bulky, soft and with a small tumour palpable on the right side. She was re-admitted to hospital on the 3rd February, 1952. Curettage was performed and obvious vesicles in small clusters were obtained. The histological report (Dr. Mary Heseltine) was as follows: "Sections of this tissue show hydatidiform mole with most marked activity of the trophoblast. This molar tissue is entirely different from the appearance of the original mole and the tissue should be regarded with the gravest suspicion."

Operation (Mr. G. Stening). 7th February, 1952

A wide total hysterectomy with bilateral salpingo-oöpherectomy was performed. At operation the uterus was found to be slightly enlarged and a tumour was seen bulging into the right broad ligament

Pathology (Dr. Mary Heseltine). Operation specimen

Macroscopic. The uterus is normal in size, measuring 8 cm. in length. Bulging out into the broad ligament on the right side is a reddish grey tumour mass, measuring approximately 2 cm. across. On incising the uterus in line with the tumour in the broad ligament, no macroscopic evidence of tumour can be seen in the uterine wall, but outside the uterine wall this tumour is found, on incision, to consist of a number of small obvious vesicles. In the ovary on the right side there is a well-developed corpus luteum surrounded by a number of small cysts.

Microscopic. Although macroscopically no vesicles could be found in the uterine wall, they are seen in the uterine wall on the same side as the extension of molar tissue which was found in the right broad ligament. In the myometrium these vesicles show very active trophoblast covering them and the nuclei of both syncytial and Langhans' cells are, in the majority of instances, bizarre in shape and giant in size. Some trophoblast can be found in a vessel. The sections taken of the tumour mass in the broad ligament again show active trophoblast covering the vesicles. Some of the tissue appears to be associated with blood vessels. In the ovary is a corpus luteum which shows changes similar to those found in a corpus luteum

of pregnancy. The diagnosis is invasive hydatidiform mole.

Follow Up

The Friedman test became negative within 2 months. Careful follow up for nearly 5 years has revealed no evidence of any recurrence.

CASE HISTORY NO. 47

Clinical Notes

This patient, a multipara aged 31, had a hydatidiform mole surgically evacuated *per vaginam* on the 9th October, 1953. The pathologist (Dr. Mary Heseltine) reported: "Sections through the molar tissue show typical hydropic vesicles and for the most part the trophoblast is relatively inactive. There were, however, some larger plaques of Langhans' cells with a little syncytium which shows some anaplasia and the cells here appear more active than usual. Using Hertig's classification this mole would probably fit into Group III or IV." Re-curette was performed on the 2nd November, 1953. At this time there had been no bleeding but the uterus was enlarged (about 12×10×5 cm.) slightly irregular and soft. The Friedman test was still positive in a dilution of 1 in 200. The curettage revealed many separate medium-sized vesicles and also large flakes of grey tissue in which no vesicles could be made out. The histological report (Dr. Mary Heseltine) stated: "(A) These sections consist of a number of typical hydatidiform vesicles all of which show active trophoblast and are associated with large plaques of trophoblast consisting of both Langhans' and syncytial cells. In comparison with the original mole the activity of the trophoblast is greatly increased. (B) These sections were taken from tissue other than that which was considered to be obviously vesicles and show areas of regenerating endometrium with solid plaques of very active trophoblast and a few small vesicles. The change in the appearance of the trophoblast between the original mole and the present tissue is very striking."

Operation (Mr. F. N. Chenhall). 13th November, 1953

In view of the recurrence of the mole with increased trophoblastic proliferation, a total hysterectomy with bilateral salpingo-oöphorectomy was performed.

Pathology (Dr. Mary Heseltine). Operation specimen (Fig. 7)

Macroscopic. The uterus is enlarged and measures 11·5 cm. overall, 8 cm. in width and 5 cm. in thickness. Both ovaries are cystic. On incising the uterus in the midline a large haemorrhagic growth is seen involving the anterior wall and in its widest part it measures 3 cm. across. It extends from the endometrial cavity to the outer third of the uterine wall.

Microscopic. Invasive mole was seen to be extending through the myometrium deep into the outer third. Many hydatidiform vesicles were present with active trophoblast surrounding them. The ovaries were cystic and luteal cells were seen to be lining the cysts.

Follow Up

On the 13th January, 1954, 2 months after the hysterectomy, examination revealed a slightly tender rounded pulsatile swelling, 5 cm. in diameter, in the right fornix and extending out to the right lateral pelvic wall. The Friedman reaction was still positive in a dilution of 1 in 200. A provisional diagnosis of a recurrence in the right broad ligament was made and a course of radiotherapy to the pelvis was advised. This was completed on the 3rd March, 1954. On the 2nd February, 1954, the patient coughed up a large clot of blood. A week later she had another haemoptysis. Radiological examination of the chest on the 3rd February, 1954 (Dr. E. H. Booth), showed "several small rounded opacities throughout the lungs and a larger one just below the left hilum, typical of metastatic growths". A further X-ray on the 10th March, 1954, showed no change. The Friedman test was still positive. The patient then returned to the country and when next seen on the 8th September, 1954, she had no symptoms and her general condition was excellent. The pulsatile mass previously noted in the right fornix was unchanged. The report of the chest X-ray stated: "The opacities previously seen are no longer apparent. The chest is clear." The Friedman reaction was negative. The patient was seen again on the 9th November, 1955. She was well and had no symptoms. The pulsatile swelling was again noted, the diagnosis of an aneurysm of the internal iliac artery was considered and when next seen on the 3rd October, 1956, confirmed by an arteriogram. On the 31st October, 1956, laparotomy was performed (Prof. John Loewenthal) and the aneurysmal sac was excised. The sac showed no evidence of any tumour or trophoblastic infiltration. The patient is now well without any sign of recurrence more than 3 years after the hysterectomy for invasive mole.

CASE HISTORY NO. 52

Clinical Notes

This patient, a para-1, aged 21, was admitted with a provisional diagnosis of hydatidiform mole. Although she had had no cough or haemoptysis, a routine radiological examination of the chest was performed. The report (Dr. E. H. Booth) read: "There are rounded opacities in the right middle and left lower zone which are strongly suggestive of secondary deposits." A provisional diagnosis of hydatidiform mole with metastases was made. On the 19th December, 1954, after induction, a hydatidiform mole was spontaneously expelled. The next day curettage was performed and more vesicles were obtained. The pathologist (Dr. Mary Heseltine) reported: "The lesion is that of a hydatidiform mole. If Hertig's classification was used the mole should be classified as Group V or probably malignant."

Operation (Mr. G. Stening). 23rd December, 1954

In view of the histology and the presence of pulmonary metastases, total hysterectomy and right salpingo-oöphorectomy was performed. The left tube and ovary were conserved.

Pathology (Dr. Mary Heseltine)

Macroscopic. The specimen consists of a uterus measuring 12 cm. in length. The endometrial lining is ragged and haemorrhagic areas extend into the wall of the uterus. There is a nodule in the broad ligament on the right side which measures 2 cm. in diameter. Vesicles of a hydatidiform mole can be seen on incising this nodule, and there are smaller vesicles surrounded by haematoma in the wall of the uterus adjacent to this nodule.

Microscopic. Sections of the nodule in the broad ligament show areas of hydatidiform mole with a considerable degree of activity of the trophoblast. The sections of the uterine wall show the characteristic appearances of an invasive hydatidiform mole. The ovary is full of small cysts lined by characteristic lutein cells.

Follow-Up

The convalescence was complicated by pyrexia and anaemia which were treated by antibiotics and blood transfusion. A further chest X-ray on the 6th January, 1955 showed "a suggestion of further rounded opacities at both bases". On the 13th January, 1955, 3 weeks after the operation, the patient coughed up a considerable amount of bright blood-stained sputum. A course of radiotherapy was given to the chest between the 17th January, 1955, and the 18th February, 1955. Further chest X-rays were taken at intervals and the reports (Dr. E. H. Booth) were as follows: 21st January, 1955 "The deposit in the right axillary region seems slightly larger"; 12th February, 1955, "The rounded opacity in the right axilla and the opacity at the left base appear unchanged but the others are not very evident now". The patient was discharged from hospital on the 22nd February, 1955. A Friedman test performed on this day was negative. On the 30th March, 1955 the patient was well. A chest X-ray showed complete disappearance of the pulmonary shadows previously noted. The Friedman reaction was again negative. This patient has been seen at intervals since and when last seen in December, 1956, 2 years after the operation, the Friedman test was negative, radiological examination of the chest revealed no abnormality, and clinically there was no sign of recurrence.

Choriocarcinoma

In this series of 64 hydatidiform moles, one patient developed choriocarcinoma, an incidence of 1·5 per cent. In Brew's series (1939) of 100 cases the incidence, as revised by Brews and Bender (1955), was 2 per cent, and, in Hertig and Sheldon's (1947) 200 cases, 2·5 per cent. Various other authorities have estimated the proportion of cases of hydatidiform mole developing choriocarcinoma from 1 per cent (Novak, 1952) to as much as 16 per cent (Essen-Möller, 1912).

Choriocarcinoma is regarded by most authorities as one of the most lethal of all malignant tumours and its great tendency to produce metastases has already been discussed earlier. Ewing (1941) says that he has never seen a survival. Novak (1953) states, however, "certainly one is not justified in saying that if a patient gets well the lesion was not a true choriocarcinoma". This statement is borne out by Novak and Seah's (1954a) unequalled follow-up of 66 proved cases of choriocarcinoma reported to the Mathieu Registry. Fifty were dead, 46 within a year, 11 (16·6 per cent) were alive after 2 years, and 5 were living after shorter periods. However, it is possible that this tumour like other malignant tumours has different degrees of malignancy. Thus some patients may die of the disease after a considerable time, so that Novak's cure rate may be less than first estimated.

The only case of choriocarcinoma occurring in this series will now be described. This was a case of choriocarcinoma developing after a hysterectomy for invasive mole.

CASE HISTORY No. 38

Clinical Notes

This patient, a primigravida, aged 23, spontaneously expelled a typical hydatidiform mole on the 23rd May, 1952. Gentle curettage was performed the next day. The report (Dr. Mary Heseltine) stated: "the lesion is that of a typical hydatidiform mole in which the villi have become hydropic and avascular. If Hertig's classification was used it would fit into Group III." A routine re-curettage was performed on the 30th May, 1952, and microscopic examination of the latter scrapings showed no chorionic villi or isolated plaques of trophoblast. A Friedman test performed on the 8th June, 1952 was negative. The patient failed to return for the follow-up examination and was not seen again until nearly 3 months later on the 20th August, 1952. She then complained of swelling of her abdomen for 2 weeks, an excessive loss at her last 2 menstrual periods and continuous slight intermenstrual bleeding. For the previous 3 days she had had a cough and on 2 occasions had had a small haemoptysis. On examination the fundus uteri was palpable midway between the umbilicus and symphysis pubis. The uterus was soft in consistency and a tumour was palpable in the left side of the organ near the left cornu. A provisional diagnosis of choriocarcinoma was made. An X-ray of the chest at this stage revealed no abnormal shadows.

Operation (Mr. G. Stening). 23rd August, 1952

Dilatation and curettage was first performed and a considerable number of typical hydatidiform vesicles was obtained. A total hysterectomy and bilateral salpingo-oöphorectomy was then performed.

Pathology (Dr. Mary Heseltine). Operation specimen (Fig. 8)

Macroscopic. The uterus is enlarged and measures 12 cm. in length. An obvious bulge is present in the fundus on the left side. On bisecting the specimen, a large invasive mole with obvious vesicle formation is seen forming a tumour mass measuring 5·5 cm. across. The vesicles can be seen invading the wall to within 1 cm. of the peritoneal surface.

Microscopic. The sections taken from the tumour mass in the fundus show extensive areas of an invasive hydatidiform mole. There is considerable activity of the trophoblast and a feature is the presence of trophoblast plus vesicles in some of the blood vessels. The activity of the trophoblast in this case shows a marked increase when compared with the original molar tissue. The invasive mole can be seen to within a short distance of the peritoneal surface of the uterus.

Follow-Up

On the 28th April, 1953, over 7 months later, she was re-admitted to hospital. She had been well since the operation until 6 weeks before. Since then she had had a most troublesome cough with much blood-stained sputum. She also complained of some loss of power in the left limbs and involuntary movements of the left arm. Examination revealed a partial left hemiplegia. Radiological examination revealed metastatic deposits scattered throughout both lungs, and the Friedman test was positive in a dilution of 1 in 200. She died in coma on the 20th May, 1953.

Autopsy Report (Dr. Mary Heseltine)

Macroscopic. Lungs: the lungs are studded at close intervals with small dark reddish purple nodules averaging 1 cm. across and slightly raised from the surface. On incising the lung tissue, these nodules are seen throughout the substance of the lung. *Liver:* the liver shows on the upper surface of the right lobe a small greyish red patch about 1 cm. across which when incised is seen to be a small haemorrhagic type of nodule about 1 cm. in depth. *Brain:* there is an obvious metastatic nodule in the posterior portion of the left parietal lobe, bulging through the surface at one point. *Pelvic floor:* the uterus, tubes and ovaries have been removed at operation. The site of operation is almost invisible save for a thin adhesion along the pelvic peritoneum.

Microscopic. The sections of lung, liver and brain show characteristic nodules of choriocarcinoma. The edge of the nodule shows malignant trophoblast in the form of both Langhans' and syncytial cells and the centre of the nodule consists of haemorrhage and necrotic tissue.

Diagnosis of Malignancy

In the follow-up of hydatidiform mole, repeated hormonal assays should be performed and correlated with the clinical findings. On occasions, diagnostic curettage is indicated. Careful evaluation of the evidence obtained from these investigations will usually show the presence or absence of invasive mole and choriocarcinoma and determine subsequent therapeutic procedure. Before a plan for the follow-up is described, the significance and value in diagnosis of these clinical, hormonal and microscopic findings will be discussed.

Original Histological Examination of Mole as Guide to Prognosis

In this hospital the histological classification of Hertig and Sheldon (1947) has been used for a number of years. They classified hydatidiform moles into 6 groups based on the degree of proliferation and anaplasia of the trophoblast. Group I is benign and Group VI is malignant. The practical value of this fine differentiation seems questionable. In this series the 1 case which developed choriocarcinoma was classified originally as Group III (possibly benign). The 4 invasive moles were initially classified as Group II, Group III or IV, Group IV and Group VI. Furthermore, Hertig (1950) himself states that half of the malignant moles (Groups V and VI) are not followed by clinical malignancy. Fredrikson (1953), and others have also described cases in which histologically low-grade benign moles have been followed some weeks later by malignancy.

Clinical Signs

The appearance or the continuation of bleeding after evacuation of the mole is usually the first clinical warning of malignancy. Care must be taken before labelling bleeding, however typical, as "menstrual" and if the biological test is still positive, curettage should always be performed without delay. Combining cases of secondary haemorrhage in this series with a very similar group in Brews' (1939) series, it seems about one patient in six will develop abnormal uterine haemorrhage after the expulsion of a hydatidiform mole and of these approximately one in three will have a complication, usually an invasive mole or occasionally a choriocarcinoma. An important sign, encountered in follow-up examinations of 3 of the 5 cases of invasive mole in the series, was the presence of

an irregularity in contour of the uterus which had not been present at earlier examination. Persistent subinvolution of the uterus often exists. At other times the first indication of the presence of choriocarcinoma may be the appearance of metastases.

Gonadotrophic Hormone Assays

Positive biological tests in high dilution are probably diagnostic of malignancy and all 5 patients in this series with Friedman tests positive in a strength of 1 in 200 after evacuation of the mole were proved to have invasive moles. A titre of this strength however, does not distinguish invasive mole from choriocarcinoma. Furthermore, these conditions may exist in the presence of a lower titre or even a negative biological test (Sutherland, 1951).

As malignancy may exist in the absence of high titres it is important to know when the biological test should become negative in uncomplicated cases following the evacuation of a mole. Hobson (1955) and King (1956) performed daily tests and found it became negative within 2 to 28 days. Occasionally the test may remain positive for longer periods and in this series in one case it did not become negative for 3 months and in another for 6 months. A possible explanation of at least some of these cases is the presence of a few villi in the uterine wall which subsequently undergo slow degeneration; that is, the case is an invasive mole of the regressive type. Another explanation offered by Mathieu (1939) and Novak and Seah (1954b) is that the lutein cysts contain the hormones and until these regress the test can be expected to remain positive. This theory cannot be supported by the findings in this series.

Although these instances occur in which a persistent positive test proves to be of no import, it is practical to regard a test still positive after 1 month with suspicion. Repeated quantitative determinations should be done to determine a rise or fall in titre and a careful assessment of the case should then be made to exclude the possibility of malignancy.

Repeat Curettage

Excluding the 17 recent cases in which re-curettage was done routinely one week after evacuation of the mole, repeat curettage was indicated in 11 patients (17 per cent) in this series. The indications were abnormal uterine haemorrhage (9 cases), clinical subinvolution of the uterus and a rising gonadotrophin titre. The curettage was performed from 2 weeks to 3 months after expulsion or evacuation of the mole. The histological findings are shown in Table IV.

TABLE IV

Histology after Delayed Curettage in 11 Cases

	Cases
Trophoblast (increased activity) and occasional villi	1
Trophoblast (increased activity) and villi (masses of fresh vesicles obvious macroscopically)	3
Regenerating proliferative endometrium ..	6
Secretory endometrium	1

What value in the detection of invasive mole and choriocarcinoma is this delayed curettage, performed 2 weeks or more after the expulsion of a hydatidiform mole? Some of the difficulties in interpretation of these curettage findings have been mentioned earlier here and have also been discussed by Novak and Seah (1954a, b) and Hertig and Mansell (1956). In this hospital however, we believe that a diagnosis of invasive mole may be made with reasonable assurance in the following cases. First is the patient from whom masses of fresh vesicles, obvious on gross examination, are obtained at a delayed curettage performed at least 2 weeks after the expulsion of a mole and provided that a thorough curettage has been performed at an earlier date. In this case a diagnosis is made purely on the macroscopic findings which we believe are strong evidence of active proliferation in the uterine wall. In only 3 patients in this series was this finding present (Case histories Nos. 32, 47 and 38) and each patient was subsequently proved to have an invasive mole. It was interesting too that in each of these cases histological examination of the trophoblastic covering of the villi showed a general "up grading" in activity from that in the original molar tissue, but it is not believed this is a necessary concomitant.

In the second type of case, curettage reveals a considerable amount of tissue which is quite uncharacteristic on macroscopic examination. Histology shows large fields of trophoblast, with both syncytial and Langhans' elements, and more or less villi which differentiate the condition from choriocarcinoma. Occasionally, as in one case in this series (Case history No. 27) sections have to be taken from a number of blocks before scattered villi are found and thus the correct diagnosis made. Such a case, however, with this excessive trophoblastic proliferation, presents little difficulty in initial management, for whether occasional villi are present or not hysterectomy is indicated.

A diagnosis of choriocarcinoma may be made with some degree of certainty in the presence of large fields of trophoblast without any trace of villous structure. However this is not an invariable finding and false negative histological findings following curettage are not uncommon. Novak and Seah (1954a) found, in cases referred to the Mathieu Registry, the diagnosis was possible following curettage in 13 cases but not until hysterectomy had been performed in another 32 cases. In the majority of these latter cases the growth was presumably in the uterine wall out of reach of the curette.

All other findings from degenerating trophoblast to normal endometrium are inconclusive, and, as in nearly all cases, the findings at this curettage should not be relied on solely in deciding further treatment but should be considered in association with the clinical findings and hormone assays.

Plan of Management for Follow Up

It is advisable in every case to perform a thorough re-curettage 7 days after the expulsion of a hydatidiform mole. Not only is this of value in removing any residual potential proliferative molar tissue accessible to the curette, but it allows a more accurate assessment of the findings should bleeding or some other sign necessitate a further curettage at a later date.

A qualitative biological test should be performed 4 weeks after the evacuation of the mole. This will most often be negative and will remain so but the test should be repeated at monthly intervals for 6 months, bi-monthly intervals for another 6 months, and then at longer intervals for another 2 years. If the test becomes positive again it is due to either another pregnancy, an invasive mole or a choriocarcinoma. To avoid this confusion the patient should be warned against becoming pregnant for at least a year after the evacuation of a mole.

If the first qualitative test is positive, quantitative determinations should be done at weekly intervals to determine whether the level of the hormone is rising or falling. Invasive mole and choriocarcinoma are suggested by a rising titre and curettage is indicated. Other indications, which may necessitate earlier curettage are secondary haemorrhage following expulsion of the mole and sub-involution or any new irregularity in contour of the uterus. All may coexist. It should be emphasized that this curettage must be thorough. A gentle scraping may simply remove necrotic tissue adhering to the uterine wall and miss more significant material underlying it.

If the material obtained with curettage, on histological examination, suggests choriocarcinoma or consists of large fields of trophoblast with occasional villi, suggesting the presence of an invasive mole, then hysterectomy is indicated. This operation is also indicated when, in the presence of suspicious clinical and hormonal findings, curettage reveals many fresh vesicles which are obvious on macroscopic examination. In such a case it is probable an invasive mole is present in the uterine wall. On the other hand, if any of the above findings are doubtful and inconclusive or if the curettage reveals degenerating trophoblast, syncytial endometritis, decidua or normal endometrium, expectant treatment should be employed. Then quantitative hormone assays once again become of great value. In managing such cases it must be remembered that sometimes invasive moles and choriocarcinoma are situated deep within the uterine wall out of reach of the curette and therefore if the uterus continues to bleed or remains subinvoluted in spite of this thorough repeat curettage and the pregnancy test remains positive, hysterectomy is indicated.

In choriocarcinoma the operation of total hysterectomy with removal of the tubes and

ovaries is adequate. Pelvic lymphadenectomy is not indicated as metastases are much more likely to occur by the vascular route than the lymphatic. Hysterectomy should not be withheld even in apparently hopeless cases with widespread metastases, as removal of the primary may be a factor in the regression or successful treatment of the metastases. In invasive mole conservation of an ovary is permissible in younger patients as metastases in this site are exceptional. Vaginal metastases should be removed if possible or irradiated. Radiotherapy, post-operatively to the pelvis in cases of choriocarcinoma and on occasions to metastases in the lungs, seems advisable. Massive oestrogen therapy in conjunction with the standard treatment has been advocated by some authorities in the belief that oestrogen may retard the growth of chorionic tissue. Despite the disappointing results to date it is essential that clinical and experimental research should continue along such lines for it is probable the ultimate cure of choriocarcinoma will prove to be either hormonal or chemical in nature.

Summary

(1) The conditions, benign hydatidiform mole, syncytial endometritis, invasive mole and choriocarcinoma are defined.

(2) The significance of benign and malignant metastases occurring in these conditions is discussed and 5 probable cases of benign pulmonary metastases are mentioned.

(3) The clinical features and methods of treatment of 64 cases of hydatidiform mole in King George V Memorial Hospital, Sydney, are analyzed and some of the findings are compared with those from other series.

(4) The complications of hydatidiform mole are mentioned. Four cases of invasive mole and 1 case of choriocarcinoma are described.

(5) Clinical, hormonal and histological findings after the evacuation of a hydatidiform mole are discussed and their value in the diagnosis of invasive mole and choriocarcinoma is assessed.

(6) A plan for the follow-up of hydatidiform mole and the subsequent management of complications is given.

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FURTHER OBSERVATIONS ON THE EXCRETION OF CHORIONIC GONADOTROPHIN BY WOMEN WITH HYDATIDIFORM MOLE

BY

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INTRODUCTION

THE excretion of chorionic gonadotrophin (C.G.) during normal and molar pregnancy was investigated recently (Hobson, 1955). Information about the excretion of C.G. by women is limited and in view of the continued use of biological tests as aids to the diagnosis of hydatidiform mole, it was felt that a further contribution to the subject would be valuable. Data have been collected about the duration of molar pregnancies, and the ovarian changes associated with them. Some information has been obtained about the concentration of C.G. in hydatidiform moles.

MATERIALS AND METHODS

Seven hundred and fifty-two specimens of urine from 314 women were examined. At the time the specimens were sent all these women were suspected of having a hydatidiform mole. The final clinical diagnosis showed that 109 of the women had a mole, and 205 of them were pregnant. The amount of C.G. in these urines was determined, semi-quantitatively and quantitatively, by two biological methods; the Hogben dilution test (Hobson, 1952), and bio-assays using groups of male *Xenopus laevis* (Hobson and Landgrebe, 1954). The response to C.G. of both male and female Xenopus was checked against a standard preparation throughout the investigation. Twenty-four hour collections of urine were not available so that all results are expressed in International Units of C.G. per litre.

Complete hydatidiform moles, from 8 women, were weighed, homogenized in 10 volumes by weight of ice-cold acetone (analytical quality), and were then placed in a refrigerator overnight. The macerated tissue was collected on a Buchner filter funnel and kept in a desiccating cabinet over phosphorus pentoxide. The mole tissue, when dry, was weighed and then reduced to a fine powder in a grinding mill. Chorionic gonadotrophin was extracted from the powdered tissue with freshly made distilled water and an all glass tissue grinder. The resulting tissue suspension was centrifuged and the residue extracted a second and a third time. The supernatant fluids were combined and assayed against a standard preparation of C.G.

RESULTS

(1) *Semi-quantitative*

Dilution tests were done on 78 urines from 45 women before the removal of the mole and on 303 urines from 205 pregnant women (Table I).

TABLE I

Amount of C.G. in Urines from 45 Women With a Hydatidiform Mole and from 205 Pregnant Women

Dilution	Undiluted	1 in 10	1 in 100	1 in 200	1 in 300	1 in 400	1 in 600
I.U.C.G. per litre ..	≒3,000	≒30,000	≒300,000	≒600,000	≒900,000	≒1,200,000	≒1,800,000
Women with mole	12	11	16	2	1	1	2
Women pregnant ..	100	93	11	0	0	1	0

The results of the dilution tests on urine from women with a hydatidiform mole showed that 16 of them were excreting about 300,000 I.U.C.G. per litre, 6 women were excreting considerably larger amounts, and 23 women excreted between 3,000 and 30,000 I.U.C.G. per litre. The urine from 2 women collected the day before the moles were aborted spontaneously contained little or no C.G. and did not produce a positive reaction when the equivalent of 30 ml. of urine was injected into each test animal. This indicates that these women were excreting less than 3,000 I.U.C.G. per litre (Hobson, 1952).

These findings were compared with the results of dilution tests done on urines from the pregnant women. Twelve of the 205 pregnant women excreted about 300,000 I.U.C.G. per litre; only one woman excreted more than this amount. A urine obtained from this patient 14 weeks after her last menstrual period (L.M.P.) contained between 1,200,000 and 1,500,000 I.U.C.G. per litre. This woman had a twin pregnancy which was later terminated because of extreme toxaemia.

Three hundred and fifty-eight specimens were obtained from 94 women after the removal of the mole. Urines from 65 of these women were received within 4 weeks of the mole having been removed. Tests on the urines from 62 of the 65 women were negative by the 4th week post-partum and in 42 of these cases the test was negative by the second week. In 3 cases the test was still positive 32, 33 and 43 days post-partum, but it was shown clinically that in these women the mole had been incompletely removed. After the removal of the retained molar tissue a negative result was obtained 4, 10 and 13 days later. Urines from 29 women were sent between the 5th and 22nd week after the removal of the mole and all were negative when tested.

(2) *Quantitative*

First morning specimens of urine, 12 ante-partum and 41 post-partum, were obtained from 6 women with a molar pregnancy. The amount of C.G. in these urines was estimated quantitatively.

In 4 women, Cases 1, 2, 3, and 5, the amount of C.G. excreted ranged from 368,000 to 1,950,000 I.U. per litre when the mole was *in situ*. The level of C.G. in the urine of 1 woman (Case 1) rose in 8 days from 1,500,000 to 1,950,000 I.U. per litre. In Case 2 there was a prolonged and increasing excretion of C.G. at a pathological level until a medical induction was attempted 17 days before the eventual abortion of the mole. Although the induction was not successful it seems likely that it established a partial separation of the mole from the uterus, as was reflected by the decreased excretion of C.G. and the eventual expulsion of the mole. The ante- and post-partum excretion of C.G. by these 4 women is shown in Figure 1.

The excretion of C.G. in these 4 cases fell until the Hogben test was negative on the 5th, 8th, 12th and 12th day post-partum.

In 2 women (Cases 4 and 6) the post-partum period was complicated by a secondary rise in the excretion of C.G. (Fig. 2). In both cases this was due to retained chorionic tissue. A considerable rise in the excretion was observed in Case 4 over a period of three days. This was followed by heavy bleeding from the vagina and an immediate drop in the excretion of C.G. The Hogben test was negative on the 20th day after the removal of the mole. The excretion of C.G. in Case 6 followed the normal post-partum pattern until the 32nd day when it was found that the amount in the urine was increasing. A total hysterectomy was performed on day 34. The Hogben test which was done a week later was negative.

(3) *Concentration of C.G. in Mole Tissue*

The amount of C.G. in hydatidiform moles from 8 women was estimated and the results expressed in I.U.C.G. per gramme, fresh and dry weight. The total concentration of C.G. in each mole was calculated from these results (Table II).

The weight of the freshly expelled moles is extremely variable and does not appear to bear any relationship to the duration of gestation. There may be some correlation between the length of gestation and the concentration of C.G. in the tissue.

It has been suggested that the concentration of C.G. is higher in the vesicular fluid of hydatid cysts than in other parts of the mole tissue (Allison, 1956), and the amount of C.G. may

TABLE II

Concentration of C.G. in 8 Hydatidiform Moles

Case	Weight of Mole—Grammes		Gestation Weeks	I.U.C.G. per Gramme		I.U.C.G. per Mole
	Fresh	Dry		Fresh	Dry	
4 ..	367·6	40·67	12	3,049	27,558	1,120,812
5 ..	330·0	45·8	14	1,986	14,309	655,380
29 ..	990·0	89·2	15	1,805	20,034	1,786,500
7 ..	338·0	36·7	17	1,426	13,133	481,998
78 ..	143·0	19·7	17	1,150	8,350	164,500
101 ..	192·0	35·8	21	623	3,340	11,955
8 ..	293·0	32·6	22	94	845	27,542
9 ..	325·0	41·2	25	72	568	23,400

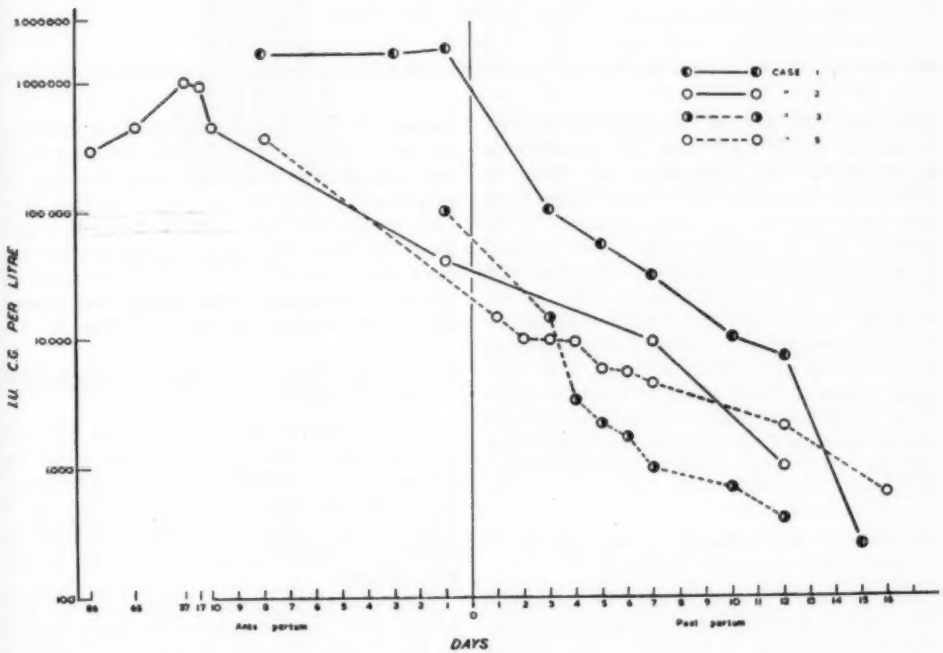

FIG. 1

Ante- and post-partum excretion of C.G. by 4 women after the complete removal of a hydatidiform mole.

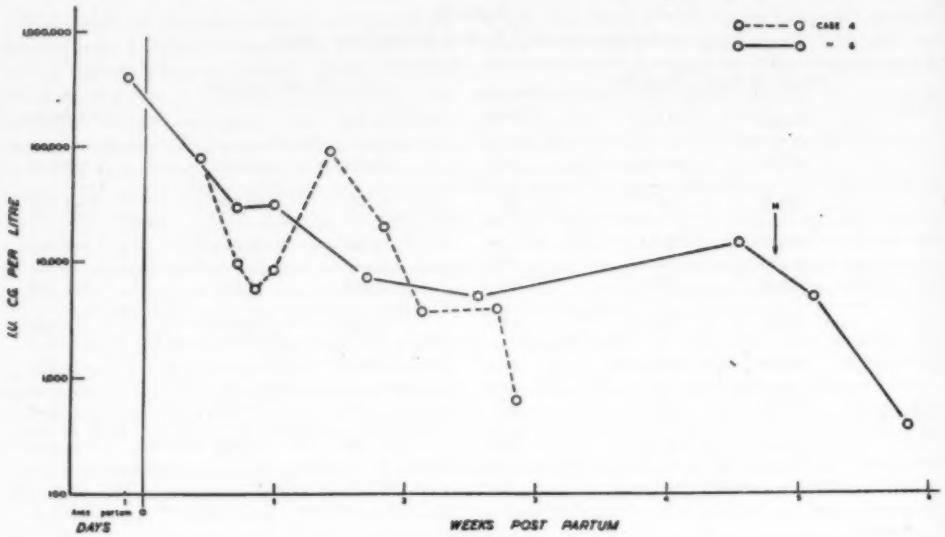

FIG. 2

The excretion of C.G. by 2 women where the removal of a hydatidiform mole was incomplete (H. Hysterectomy).

vary from one part of the mole to another, depending upon the extent of hydatidiform degeneration. This assumption was tested by dividing up one mole, Case 4, into 4 pieces. Each piece was weighed, dried, and reduced to a fine powder. The 4 powders were first assayed separately and then combined by mixing and re-assayed. The concentration of C.G. in the 4 pieces varied between 23,825 and 38,200 I.U.C.G. per gramme of acetone dried tissue, with a mean value of 29,146±5,650 I.U. The combined assays of the 4 pieces of tissue, and the assay on the powders after mixing gave the total concentration of C.G. in the mole as 1,188,736± 226,716 I.U. and 1,120,812±197,145 I.U. respectively.

(4) *Gestation and Spontaneous Abortion in Molar and Non-molar Pregnancy*

One hundred and one out of 214 women who had a molar pregnancy aborted spontaneously. The mean duration of gestation in the women who aborted spontaneously was 130±40 days, the range was from 47 to 259 days. For comparison the time at which spontaneous abortion occurred during pregnancy was obtained from our laboratory records. The mean duration of pregnancy in 75 women who aborted was 124±39 days and the range was from 35 to 231 days. The length of gestation in both groups was calculated from the L.M.P. The percentage of abortions occurring in these groups was plotted against the duration of gestation (Fig. 3).

(5) *Ovarian Changes Associated with Normal and Molar Pregnancy*

One hundred and seventy-six women who had a hydatidiform mole were examined either by palpation or at hysterotomy for the presence of lutein ovarian cysts. They were present in 41 women. Lutein cysts were mainly unilateral in occurrence though in some women both ovaries were affected.

The presence or absence of lutein cysts in 171 women with normal pregnancies was recorded by the clinician. Ovarian cysts were present in 8 women, and in one woman both ovaries were cystic.

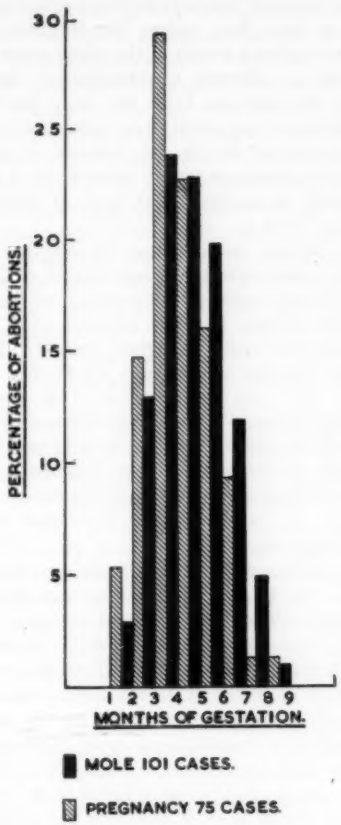

FIG. 3

Distribution of spontaneous abortions by length of gestation.

DISCUSSION

It has been shown that the amount of C.G. excreted by women with either a normal pregnancy or a hydatidiform mole is extremely variable and that the result of a single dilution test as a means of distinguishing between a normal and a pathological pregnancy is of little value. During normal pregnancy the excretion of C.G. rises to a maximum peak level of 450,000 I.U. and falls to a maximum of 30,000 I.U. per litre (Hobson, 1955). The only time when a single estimation might be of value is when the excretion is higher than 600,000 I.U.C.G. per litre during the 1st to the 4th months of pregnancy, or higher than 300,000 I.U. between the 5th and final months of pregnancy. If there are clinical reasons for suspecting the presence of a hydatidiform mole then such a high level of C.G. should be considered as confirmatory evidence since, with a very few exceptions, they are higher than the levels of C.G. recorded for normal pregnancy.

Hamburger (1944) reported a case of a single pregnancy in which the peak excretion was 900,000 I.U.C.G. per litre, and values as high as 450,000 I.U. per 24 hours have occasionally been reported (Smith, Albert and Randall, 1951; Jones, 1954). All these estimations were done in the first 4 months of pregnancy and such high levels of C.G. in the urine are unusual. In this series one woman with a twin pregnancy was excreting between 1,200,000 and 1,500,000 I.U.C.G. per litre at the 14th week of pregnancy. The excretion of C.G. at this level is greater than any that has been recorded previously for a pregnancy, but it serves to emphasize the fact that even when such an extremely high level of excretion of C.G. is found this information can only be used in conjunction with the clinical findings.

The peak excretion of C.G. in normal pregnancy usually occurs between the 6th and 14th week. Owing to the difficulties of knowing exactly how long the menstrual cycle is in any individual, it is probably safer to assume that a peak may be expected between the 4th and the 16th week. After this time the level of C.G. excretion falls fairly rapidly to between 3,000 and 30,000 I.U. per litre (Hobson, 1955) and is maintained at this level until the end of pregnancy. For this reason the pattern of C.G. excretion may serve to distinguish between the presence of a hydatidiform mole and a normal pregnancy. If the level of C.G. excretion after the 16th week does not fall or increases it implies that a mole may be present. It follows that assays done on specimens of urine sent over a period of a week or so are far more useful as a diagnostic aid than the result obtained from a single specimen.

As will be seen from Table I a low level of C.G. excretion or even a negative result does not exclude the presence of mole tissue. Urine from 2 women in this series, collected 1 day before they spontaneously aborted a mole, did not contain enough C.G. to produce a positive Hogben test. This suggests that these moles may have separated from the uterus before the test was done.

It has been shown that the biological test becomes negative within 4 weeks after the removal of all tissue producing C.G. (Hobson, 1955). In Case 6 (Fig. 2), following the abortion of a hydatidiform mole, the excretion of C.G. decreased until the 19th day post-partum. Between the 19th and 32nd day the urinary level of C.G. rose to 13,600 I.U. per litre, an increase of 7,890 I.U. in less than 2 weeks. The patient was 42 years old, and, in view of the continued and increased excretion of C.G. and the fact that the pathologist had reported that the original mole "shows a rather marked degree of trophoblastic activity", a hysterectomy was done. The Hogben test was negative 7 days after the hysterectomy. Examination of the uterus showed that some active chorionic tissue was present which had invaded the myometrium. Only the continued excretion of C.G. showed that the mole had not completely aborted.

A negative Hogben test was obtained with the urine from 62 women within 4 weeks of the mole being removed. Hogben tests for 3 other women were positive at this time, and, when their uteri were evacuated between the 4th and 6th week after the first attempt to remove the mole, the Hogben tests were negative 2 weeks later.

A negative Hogben result was obtained with the urine of 42 of the 65 women within 2 weeks of the removal of the mole, and it is possible that if complete removal is accomplished the test would always be negative after this interval of time. There is a wide variation in the time between the removal of the mole and the time when the urine contains no C.G. and it is difficult to be certain that fragments of chorionic tissue are not retained in some cases after the first removal. The remaining chorionic tissue may regress or abort spontaneously during the first weeks post-partum.

The results of this and previous investigations make it clear that, unless the Hogben test is negative within 4 weeks of the whole mole being removed or aborted spontaneously, the prolonged excretion of C.G. can only be due to retained chorionic tissue. This indicates the need for systematic follow up because a choriocarcinoma develops more often from a molar pregnancy than any other type of pregnancy (Hertig, 1950).

The present investigation shows that there may be a decline in the concentration of C.G. in hydatidiform moles as the duration of gestation increases (Table II). The amount of C.G. in hydatidiform moles is highest between the 3rd and 4th months of gestation. Diczfalusy (1953) found that the concentration of C.G. in placentae reached a maximum between the 2nd and 3rd months of gestation and afterwards declined to a low level. The concentration of C.G. in the pathological tissue at all stages of gestation is much greater than that of the normal placenta.

In a previous investigation the concentration of C.G. in 7 incomplete moles was estimated (Hobson, 1955). No correlation was found between the concentration of C.G. in extracts of mole tissue, the level of C.G. in the urine or the length of gestation. It was suggested that the existence of such a relationship would perhaps be revealed if hydatidiform moles were assayed in their entirety and not in part. The results of the bioassays on 4 pieces of tissue from different areas of the same mole illustrate the differences in the concentration of C.G. that can be found.

Figure 3 shows that the time during gestation at which spontaneous abortions in women with molar and non-molar pregnancies occurs is not significantly different, being 130 ± 40 days and 124 ± 39 days respectively. The majority of abortions in both groups occurred between the 3rd and 5th months of pregnancy. These findings are in agreement with the observations made by Huber and Hörmann (1954) and Smalbraak (1957) about the duration of molar pregnancy. The almost identical distribution of abortions in molar and non-molar pregnancies suggests that the factors responsible for the evacuation of the uterus in both groups may be similar.

Data collected in this investigation showed that cystic ovaries occurred once in every 4 molar pregnancies compared with once in every 21 cases of normal pregnancy. The incidence of cystic ovaries in women with a hydatidiform mole is extremely variable. Sherman (1935) and Smalbraak (1957) reported it to be one in 25 and Patellani (1905) one in 1·1 molar pregnancies. Although the occurrence of cystic ovaries in our two groups was significantly different, the wide variation reported by other workers suggests that the presence or absence of cystic ovaries makes no contribution to the diagnosis of hydatidiform mole.

Summary

(1) The concentration of C.G. in urine and mole tissue was estimated by two methods, a semi-quantitative one using female *Xenopus laevis* and a quantitative one using groups of male *Xenopus laevis*.

(2) Data are presented on the ante- and post-partum excretion of C.G. by 109 women with a hydatidiform mole and 205 pregnant women, and the amount of C.G. in 8 complete hydatidiform moles has been estimated. The usefulness of these estimations for diagnostic purposes is discussed.

(3) It is shown that the time during gestation at which spontaneous abortions in women with molar and non-molar pregnancies occurs is not significantly different. It is suggested that the factors responsible for the evacuation of the uterus in both groups may be similar.

(4) Cystic ovaries occurred in 23 per cent of the women with a molar pregnancy compared with 4·7 per cent of women with a normal pregnancy, but in view of the wide variation in the occurrence of cystic ovaries in molar pregnancy reported by various authorities, it is concluded that their presence or absence makes no contribution to the diagnosis of hydatidiform mole.

(5) When hydatidiform moles are completely evacuated negative Hogben tests are to be expected within 4 weeks. Incomplete removal or abortion of the mole results in the Hogben test remaining positive until the retained chorionic tissue is removed or aborted.

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ANTIHISTAMINICS IN THE MANAGEMENT OF ABORTION

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IT is estimated that 1 in every 5 pregnancies ends in abortion. Apart from the grave risks to life and health of mothers, abortions cause a foetal loss estimated to be more than double that due to stillbirths, neonatal death and infant mortality combined. Besides, repetition of miscarriages results in frustrations which may cause a state of nervous tension with, perhaps, grave psychological sequelae.

Many aetiological factors have been blamed. Apart from well defined causes such as syphilis, hypertension, chronic nephritis, pathological conditions in the ova as well as uterine anomalies, malpositions and incompetence of the internal cervical os there is a big group of cases in which the aetiological factor is not clear. Hormonal imbalance with deficiency of oestrogen, progesterone and/or chorionic gonadotrophin, low basal metabolism, dietetic deficiencies and psychosomatic disturbances have been also considered as possible causative factors.

Any causative agent in abortion may act in one or both of two ways: (1) either it may lead to death of the ovum and this is followed by its expulsion or, (2) it may lead to abnormal uterine activity expelling a healthy ovum. Such abnormal uterine activity might be induced by the circulation in the blood of an oxytocic substance. Histamine produces contraction of the smooth muscle throughout the body. It is known that the uterus of the cat, rabbit and guinea-pig are strongly contracted by very small amounts of histamine. The uterus of the rat, however, is relaxed by the drug. The human excised uterus is contracted by histamine and, when the drug is injected, the parturient or post-partum uterus is promptly and strongly contracted.

During pregnancy the histaminolytic power of the serum increases more than one thousand times (Ahlmark and Werko, 1950); histaminase increases sharply from the end of the second month to the end of the fifth month, and continues in a rising level up to term. The purpose of this increased histaminase production is not known with certainty but quite logically it might be to counterbalance an increased production of histamine during pregnancy. Such increased production might exceed the physiological limits leading to a high level of histamine in the blood which might excite uterine contractions.

The oxytocic effect of histamine can be blocked by antihistaminics, although these may not inhibit the spontaneous contractions of the organ.

The purpose of this investigation is to apply this theoretical conception of the action of histamine on the uterus to the problem of abortions assuming that in cases of single or repeated abortions there might be a pathological condition leading to increased histamine content in the plasma without sufficient parallel increase in histaminase production, with consequent contractions of the uterus and expulsion of the ovum.

Kapeller-Adler (1950), quoting Walentin (1945), mentioned that in threatened abortion, where the pregnancy continued and ended with the birth of a living child, the histaminase values were normal or just on the lower border

of normal. In the cases ending in abortion the histaminase content of the serum was far below this border. There were, however, a few exceptions to this rule and it was observed that some cases ending in abortion had rising histaminase values even after expulsion of the ovum.

Anrep, Barsoum and Ibrahim (1947), stated that in suspected intra-uterine death of the foetus, the histaminase reaction is useful as a guide to prognosis of a given case: cases where the diminution of the histaminolytic index was about a half or less than that expected for the month of pregnancy usually ended in termination of the pregnancy. Especially unfavourable are those cases in which the power of the serum to inactivate histamine progressively diminishes in the course of a few days or even hours. A diminution of the histaminolytic index by less than 40 per cent of the expected result, especially when it shows a tendency to increase in the course of a few days, implies a good prognosis.

Reports have been made of cases of threatened and habitual abortions treated by antihistaminics with good results.

Saurer in 1946 suggested the use of an antihistaminic preparation in threatened abortion. Luisi (1949) reported favourably on their use. Hirzfeld and Krystoporski (1950) reported on their trial in cases of abortion on the assumption that abortion might be of allergic origin with increased histamine production; he had a salvage rate of 74 per cent in cases treated in this way.

Herrod (1953) has reported 2 cases of habitual abortion coming under his care. One of these had bleeding which was quickly controlled by Benadryl, but after cessation of its administration abortion occurred; in the other case the patient had severe bleeding with cramps in the lower abdomen which were quickly controlled by Pyribenzamine. These recurred when Pyribenzamine was withheld and so he had to repeat the dose and the pregnancy continued.

Favourable results have been also claimed by Latinek (1953) and Sora (1954).

Material and Methods

Fifty cases of threatened abortion were admitted to the Kasr el Aini Hospital as emergency cases. Of these cases 15 were cases of habitual abortion, that is, they had 3 previous abortions or more according to the definition suggested by Malpas.

The remaining 35 cases had had no abortions or one abortion only. Cases who have had 2 abortions were excluded from the series because they could not be considered as genuine habitual aborters. Each patient admitted was carefully interrogated, especially as regards duration and history of syphilis; the urine was examined for albumin, sugar and casts and the Wassermann reaction was done.

On admission, 10 ml. of blood is drawn from the cubital vein into a centrifuge tube containing one milligramme of heparin. The blood is centrifuged and the plasma is drawn carefully for the determination of its histamine equivalent, since according to Anrep *et al.* the plasma histamine is the active part of the blood histamine, the portion which is in the red blood corpuscles, although much higher than that in plasma, is inactive and is firmly retained by the corpuscles. The histamine equivalent of the plasma is determined according to the method of Barsoum and Gaddum (1935), modified by Anrep, Barsoum, Talaat and Wieninger (1939). A portion of the plasma is separated after centrifuge for the determination of the histaminolytic index according to the method described by Anrep *et al.* (1947).

The patient is confined to bed and given Pyribenzamine which is a powerful antihistaminic related to Benadryl but which contains a pyridine nucleus. Mayer, Huttrer and Scholz (1945) have found that Pyribenzamine is capable of antagonizing efficiently the action of histamine on the intestine and uterus of rabbits and guinea-pigs.

The Pyribenzamine is given in tablet form (each tablet containing 50 mg.). The treatment is started with three tablets daily until bleeding has stopped completely; thereafter it is given in a dose of one tablet daily. The duration of administration is prescribed tentatively for, as we shall see, some cases aborted within 40 hours of the stoppage of the Pyribenzamine treatment. To check the antihistaminic effect of Pyribenzamine, another blood sample is taken 2 days after the end of treatment, and the level of plasma histamine and the histaminolytic index

TABLE I

Case Number	Week of Gestation	Number of Previous Abortions	Number of Days of Medication	Duration of Bleeding After Start of Treatment	Histaminolytic Index Before Treatment	Histaminolytic Index After Treatment	Plasma Histamine Before Treatment	Plasma Histamine After Treatment	Result
					Per cent	Per cent	Microgramme/ml.	Microgramme/ml.	
1	16	10	12	1	30	40	0·06	0·028	Pregnancy continued
2	24	3	10	5	30	75	0·13	0·035	Pregnancy continued
3	12	3	17	1	20	30	0·125	0·03	Pregnancy continued
4	20	4	2	2	30	50	0·06	0·04	Abortion after two days
5	12	5	18	2	10	—	0·09	—	Pregnancy continued
6	8	8	13	3	Not detected	10	0·075	0·032	Pregnancy continued
7	14	3	13	1	10	30	0·19	0·1	Pregnancy continued
8	8	4	18	2	Not detected	12	0·115	0·06	Pregnancy continued
9	12	3	13	1	12	30	0·15	0·05	Pregnancy continued
10	12	3	14	1	10	28	0·1	0·04	Pregnancy continued
11	12	3	5	2	8	25	0·125	0·06	Pregnancy continued
12	8	3	11	11	Not detected	12	0·1	0·04	Pregnancy continued
13	20	3	13	1	20	50	0·2	0·07	Pregnancy continued
14	22	8	13	5	20	54	0·05	0·032	Pregnancy continued
15	8	3	11	2	Not detected	10	0·4	0·15	Pregnancy continued

are estimated. When bleeding stops the patient stays in hospital for one week free of bleeding and is then discharged if not belonging to the group of habitual aborters. Cases of habitual abortion, however, are hospitalized till the end of 28 weeks.

One hundred and seventy-five cases of threatened abortion (both habitual and non-habitual), admitted to hospital during a period of 12 months before the commencement of this investigation, were used as a control series. Of these 175 cases of threatened abortions, 52 were habitual aborters and 120 were not. These cases were treated by rest in bed, sedatives (Bromides and Luminal) and by Progesterone. Of the 2nd group of 120 cases of threatened abortions 66 continued their pregnancy, that is a foetal salvage rate of 55 per cent, but of the 52 cases of habitual abortions only 17 continued their pregnancy, that is a foetal salvage rate of 30·68 per cent.

The level of histamine in the plasma and the histaminolytic index were estimated in 20 cases of normal pregnancy to determine the average normal for these cases and to compare it with the series of threatened abortion.

RESULTS

Group A: Cases of Habitual Abortion

In all 15 cases of habitual abortion the plasma histamine was raised to many times its normal level and in all this high level was brought down by Pyribenzamine and in all cases but one (Case 4) the pregnancy continued till term. This gives a foetal salvage rate of 93·3 per cent. In similar cases treated by rest, sedatives and progesterone the pregnancy continued in 17 out of 52 cases, a foetal salvage rate of 30·68 per cent. (Table I.)

Group B: Cases of Threatened Abortion with no History of Abortion or with History of One Single Abortion

This group (Table II) consisted of 35 cases of threatened abortion. The pregnancy was successful in 22 cases. In 5 cases the bleeding stopped so long as the antihistaminic was administered but when its administration was stopped bleeding started again and abortion quickly occurred.

It may be interesting to recite the history of two of these cases.

TABLE II

Case Number	Week of Gestation	Number of Previous Abortions	Number of Days Medication Taken	Plasma Histamine Before Treatment mg./ml.	Plasma Histamine After Treatment mg./ml.	Duration of Bleeding After Beginning of Treatment	Result
1	10	0	15	0·286	0·035	15	Abortion completed.
2	10	0	17	0·375	0·021	5	Pregnancy continued.
3	8	0	12	0·05	0·015	3	Pregnancy continued then abortion occurred three days after discharge.
4	20	1	13	0·055	0·013	5	Pregnancy continued.
5	16	0	6	0·09	0·05	2	Pregnancy continued but abortion occurred two days after discharge.
6	12	0	21	0·125	0·06	6	Pregnancy continued.
7	12	0	8	0·1	0·075	8	Abortion completed.
8	10	0	2	0·13	—	2	Abortion became inevitable and evacuation was done.
9	22	0	3	0·05	—	3	Abortion completed.
10	14	1	8	0·09	0·08	2	Pregnancy continued but abortion occurred two days after.
11	12	1	8	0·1	0·04	2	Pregnancy continued.
12	8	0	15	0·05	0·02	5	Pregnancy continued.
13	14	0	15	0·09	0·07	2	Pregnancy continued.
14	16	0	2	0·06	—	2	Abortion completed.
15	14	0	6	0·125	0·10	1	Pregnancy continued.
16	12	0	12	0·15	0·05	1	Pregnancy continued.
17	8	0	10	0·125	0·10	4	Pregnancy continued.
18	16	0	22	0·2	0·05	12	Pregnancy continued.
19	12	0	8	0·25	—	7	Abortion occurred.
20	12	1	9	0·22	0·05	4	Abortion occurred.
21	8	0	12	0·2	0·05	1	Pregnancy continued.
22	12	0	11	0·35	0·07	2	Pregnancy continued.
23	20	0	5	0·5	0·4	1	Abortion occurred two days after discharge.
24	8	0	4	0·3	0·5	4	Abortion completed.
25	12	0	8	0·3	0·5	4	Pregnancy continued.
26	16	0	8	0·2	0·06	1	Pregnancy continued.
27	12	0	6	0·15	0·10	3	Pregnancy continued.
28	20	0	5	0·225	0·08	1	Pregnancy continued.
29	8	0	8	0·33	0·065	1	Pregnancy continued.
30	12	0	8	0·175	0·05	1	Pregnancy continued.

Case 3

The patient, a 4-gravida, 28 years old, was complaining of bleeding *per vaginam* for 10 days. She had had amenorrhoea for 8 weeks. The uterus was enlarged in correspondence to the period of amenorrhoea. The urine was sugar- and albumin-free and the Wassermann reaction was negative. The patient was put to bed and given Pyribenzamine, one tablet 3 times daily. The bleeding stopped in 24 hours. The Pyribenzamine was continued in the same dosage for 3 days more. Thereafter one tablet was given each night for 9 days, during which time the patient was free from bleeding and pain. She was discharged from hospital but returned after 2 days complaining of bleeding and colic. On examination the cervix was found to be dilated and the ovum was felt through it. Four hours after re-admission, abortion was completed.

Case 5

This patient, a 5-gravida, aged 30 years, married for 12 years, had had 4 full-term normal labours, and one abortion 8 months previously. She had had amenorrhoea for 16 weeks with bleeding *per vaginam* for 2 days before admission. She complained also of lower abdominal pain.

On examination the uterus was of a size corresponding to that of the amenorrhoea and the cervix was closed. A blood sample was taken and the result was as follows: Plasma histamine 0·09 (average normal 0·02 μmg.), histaminolytic index: 12 per cent (average normal for that duration 35 per cent). Pyribenzamine was given in a dose of one tablet 3 times daily, then one tablet daily for another 3 days. Twenty-four hours after stoppage of Pyribenzamine bleeding recurred and the abortion was completed.

Normal Pregnancy

The level of plasma histamine and the histaminolytic index were determined in 20 cases of normal pregnancies, the duration of which varied from 8 to 20 weeks. The plasma histamine varied between 0·012 μmg. and 0·030 μmg./millilitre with an average of 0·02 μmg./millilitre. The histaminolytic index showed values which increased with the period of gestation. Considering the normal level at full term to be 100 per cent we got the average normal following results.

At	8 weeks	..	10 per cent.
	12 weeks	..	25 per cent.
	16 weeks	..	35 per cent.
	20 weeks	..	45 per cent.

Discussion

Certain facts could be deduced from the present investigation:

(1) In almost all cases of threatened abortion in which recognizable causes were excluded there is a high level of plasma histamine with diminution in the level of plasma histaminase.

(2) The administration of an antihistaminic (Pyribenzamine) in these cases can bring down the level of plasma histamine substantially.

(3) Such administration improves the foetal salvage rate in these cases, to a lesser extent in single aborters than in cases of repeated abortions where the foetal salvage rate is significantly raised.

(4) The administration of the antihistaminics in reduced doses should continue for a long time, probably several weeks after the onset of bleeding or pain to guard against the recurrence of abortion. This has been observed on many occasions during the present investigation a short time after stoppage of administration of the antihistaminics.

(5) The absence of detectable histaminase in the serum after the tenth week denotes a bad prognosis for the pregnancy; we have 5 cases in this series in which the histaminolytic index was not detected which all ended in abortion.

This could be explained by a high level of histamine in the blood unopposed by histaminase leading to irritation of the uterus and abortion.

The fact that administration of the antihistaminic Pyribenzamine is more effective in habitual abortion (a foetal salvage rate of 93·3 per cent compared to 30·68 per cent obtained in cases treated by sedatives and progesterone), than in cases of simple threatened abortion (a foetal salvage rate of 62 per cent compared with 55 per cent in cases treated by sedatives and progesterone), suggests that the histamine role might be operating to a much greater extent in cases of habitual abortion than in other cases of abortion. A possible explanation is that, in cases which are not habitual aborters, an important cause for these abortions is a malformation in the ovum. In such cases the antihistaminics will naturally be of no value.

We think that in the case of habitual abortions the plasma histamine level and the histaminolytic index should be determined as a routine investigation. Cases in which the histaminolytic index is low or the plasma histamine is high should have an antihistaminic administered especially at the expected time of abortion and the antihistaminic administration should continue for a few weeks in cases in which abortion is threatening to avoid the effect of a possible increase in histamine level after withdrawal of the antihistaminic.

Summary

(1) The plasma histamine and the histaminolytic index have been determined in 50 cases of threatened abortion. Of these cases, 15 were habitual aborters.

(2) In all 50 cases the plasma histamine was raised and the histaminolytic index was lowered.

(3) Pyribenzamine lowered the level of plasma histamine in all cases.

(4) The foetal salvage rate has been much raised in cases of habitual abortions as compared to control cases.

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PHYSIOLOGICAL ANAEMIA OF PREGNANCY

A Plea for the Abolition of this Term

BY

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THE term "physiological anaemia of pregnancy" can be regarded as dating back to Strauss (1934), who considered that an apparent anaemia could occur in pregnancy as a result of blood dilution or hydraemia. This increase in the blood volume during pregnancy was no new observation; but, while earlier reports were rather conflicting, the classical paper of Dieckmann and Wegner (1934) established an average increase of 23 per cent.

The tendency today is to speak of "physiological hydraemia of pregnancy" rather than anaemia, the basic concept remaining the same as twenty years ago. It has, however, been observed that this blood dilution is an inconstant finding (Boycott, 1936) and that, shortly before the onset of labour, there is usually an appreciable diminution in the hydraemia (Caton *et al.*, 1949). Such observations tend to evoke doubts as to whether this anaemia can rightly be called physiological. Moreover, several reports have been appearing recently to demonstrate that these lower haemoglobin levels occurring in pregnancy can almost always be corrected by means of adequate iron therapy (Davis and Jennison, 1954; Fisher and Biggs, 1955). The misgiving consequently arises that this condition could, after all, be an actual anaemia, the clinical features of which could be easily missed.

In an attempt to study this problem, a detailed review of the relevant literature has been carried out. The results of a limited investigation are at the same time presented in order to point out the large number of anaemic pregnant women left untreated when their condition remains attributed to the so-called physiological hydraemia of pregnancy.

INVESTIGATION

(a) *Material*

The number of patients investigated was 183. This comprised 148 antenatal cases between the 23rd week and term, and 35 cases within the first fortnight of the puerperium. All these patients were referred to our Obstetric Department as "normal" cases. In no mother was there any clinical evidence of anaemia or any obstetric or other complication that might predispose to anaemia. No reference is made to parity.

The blood of the last 30 patients in the series was investigated more fully than the rest with regard to absolute values. These values are part of a more comprehensive research at present being carried out with the purpose of establishing the local incidence of anaemia in pregnancy and studying any possible changes in the blood picture occurring in the course of pregnancy.

(b) *Method*

The haemoglobin was estimated in all cases by the acid haematin method of Sahli, a reading of 100 per cent corresponding to 14·8 g. per 100 ml. blood (revised Haldane scale).

The haematological investigations on the 30 patients consisted of the haemoglobin level, the red cell count, and the packed cell volume (P.C.V.). From these values were calculated the mean corpuscular volume (M.C.V.), the mean corpuscular haemoglobin (M.C.H.), and the mean corpuscular haemoglobin concentration (M.C.H.C.). No bone marrow smears were done.

(c) *Findings*

The distribution of the haemoglobin values is shown in Table I, the cases being subdivided into

TABLE I

Hb. Per Cent	Weeks of Pregnancy							1 or 2 Weeks Post-partum
	23 or less	24–27	28–31	32–35	36–38	39–41	42 or more	
Over 100 ..	–	–	–	–	1	2	–	1
91 to 100 ..	–	–	1	1	8	6	1	2
86 to 90 ..	1	–	2	1	10	7	2	2
81 to 85 ..	2	2	3	7	10	10	2	5
76 to 80 ..	2	2	1	10	7	8	2	7
71 to 75 ..	–	1	2	4	4	7	–	7
61 to 70 ..	–	–	–	3	2	8	1	8
60 or less ..	1	–	–	–	2	2	–	3
Total	6	5	9	26	44	50	8	35

groups according to the period of gestation in weeks. It will be seen, for example, that out of the 50 cases at term (39 to 41 weeks) the haemoglobin level was above 90 per cent in only 8 cases (16 per cent).

In Table II the cases are considered in three groups only—antenatal, postnatal and total. If we follow the common practice of accepting 10 g. haemoglobin per 100 ml. blood (68 per cent Haldane) as the lower limit for physiological anaemia of pregnancy, then the incidence of anaemia in this series would comprise 19 antenatal cases (13 per cent) and 11 postnatal cases (31 per cent), amounting to a total of 30 cases (16 per cent). If, however, this limit is raised to 12 g. haemoglobin per 100 ml. blood (81 per cent Haldane), then the number of anaemic patients assumes disquieting proportions: 69 antenatal cases (47 per cent) and 25 postnatal cases (71 per cent), a total of 94 cases (51 per cent). This not inconsiderable difference in the accepted incidence of anaemia resulting from a raising of the haemoglobin standard from 10 g. to 12 g. per 100 ml. blood demands active consideration.

TABLE II

Hb Per Cent	Antenatal	Postnatal	Total
Over 100 ..	3	1	4
91 to 100 ..	17	2	19
86 to 90 ..	23	2	25
81 to 85 ..	36	5	41
76 to 80 ..	32	7	39
71 to 75 ..	18	7	25
61 to 70 ..	14	8	22
60 or less ..	5	3	8
Total ..	148	35	183

The detailed haematological findings of 30 cases (26 antenatal and 4 postnatal) are shown in Table III. The cases are again subdivided into groups according to their period of gestation, the second column indicating the number of cases in each group. The remaining columns give the average reading of each separate group for the various investigations.

The local prevalence of iron deficiency in the general population has not been studied, so that it is not possible to compare the haemoglobin level in pregnancy with that of non-pregnant controls. No attempt is made to draw any conclusions from the Tables presented, but an overall tendency to anaemia is at once evident. This is especially noticeable in the low readings obtained for the mean corpuscular haemoglobin concentration.

DISCUSSION

It is no easy matter to study anaemia in pregnancy—to define its limits, investigate its incidence, assess its treatment. Hence reports are often conflicting. Thus, from London, Boycott (1936) reported that 22 per cent of his unselected cases had a haemoglobin level of less than 11 g. per 100 ml.; and Jerlov (1927) in Denmark found that 25·9 per cent of his patients had less than 10·5 g. haemoglobin per 100 ml. blood. More recently, Benstead and Theobald (1952) investigated 2,000 consecutive cases, the haemo-

TABLE III

Weeks of Pregnancy	No. of Cases	Hb. g./100 ml.	R.B.C. Per c.mm.	P.C.V. Per cent	M.C.V. c.μ	M.C.H. μμg.	M.C.H.C. Per cent
24–27	2	11·2	4,200,000	38	90	26·6	29·4
29–31	4	12·1	4,300,000	37	88	28·3	32·6
33–35	6	11·3	4,000,000	37	91	28·2	31·5
38	5	11·7	4,500,000	40	89	26·3	29·4
40	5	11·5	4,300,000	39	90	27·1	29·9
42	4	12·1	4,000,000	38	96	31·7	32·0
Total antenatal ..	26	11·7	4,200,000	38	91	28·0	30·9
1–2 week postnatal	4	10·7	3,800,000	34	91	28·6	31·5
Total	30	11·5	4,200,000	37	91	28·1	31·0

globin level being less than 12 g. in 40·15 per cent, and less than 10 g. in 6·55 per cent; it is worth noting that these levels were calculated at the 16th week of pregnancy, i.e., before the occurrence of any significant haemodilution. In America Rath and others (1950) did not discover a single case of iron deficiency in their pregnant patients; whereas Holly (1955) found that only 21·8 per cent of his patients maintained their initial pregnancy levels if iron was not added to their diet.

Difficulty and disagreement arise also in the assessment of the dangers associated with anaemia in pregnancy. Boycott (1936) concluded that this anaemia probably was not a serious risk in England, and Magee and Milligan (1951) even doubted the advantages in raising the haemoglobin level during pregnancy by iron therapy. In the opinion of Browne and Browne (1955, p. 468) there is little risk if the haemoglobin is above 7·4 g. per 100 ml., the danger being great only when this level falls below 4·4 g. Over-confidence seems to have no limits: Tasker *et al.* (1956) go so far as to imply that one need not be perturbed in allowing a patient to go into labour with a haemoglobin level between 3 and 5 g. per cent. One wonders at what level it could be said that such teaching became pernicious. The impression is further gained that this teaching pays no regard to the fact that, at these low haemoglobin levels, the iron stores of the body are at the same time very much depleted, or practically non-existent. It is only too obvious that with a full complement of haemoglobin the woman in labour is in the best possible position to withstand blood loss, normal or abnormal. Infection, too, is thereby better resisted. No wonder that a high haemoglobin level in the pregnant patient instils greater confidence within the doctor and midwife —a confidence that is highly important in obstetrics, particularly in domiciliary practice. In pointing out this factor, Fisher and Biggs (1955) also believed that, at the higher levels of haemoglobin, the mothers are more energetic and tire less easily. The influence of anaemia on labour has not been adequately studied, but there have been reports suggesting a higher incidence of primary uterine inertia (McCormick 1944) and of prolonged labour (Traylor and Torpin, 1951; Briscoe, 1952). In the puerperium anaemia is apt to interfere with breast-feeding and it predisposes to sepsis (Cope *et al.*, 1956). Its prevention, therefore, ensures for the woman a quicker recovery from childbirth and gives her more energy to enjoy motherhood and to resume her household duties (*British Medical Journal*, 1955).

The babies of mothers who had iron deficiency during pregnancy do not seem to have a tendency to develop neonatal anaemia (Wolff and Limarzi, 1949; Woodruff and Bridgeforth, 1953). The foetus has a greater avidity for any available iron than the mother, as its erythropoiesis is much more active: as a result the baby at birth rarely has any haemoglobin deficiency. However, in the presence of maternal anaemia the iron stores of the foetus may not always be replete so that these stores may be expected to become exhausted before the normal period of 3 to 6 months. Strauss (1933) has demonstrated a correlation between the mother's

haemoglobin level during pregnancy and her infant's haemoglobin level some months after birth. This corroborates the findings of Mackay (1931) and of Parsons (1946) in connexion with the relation of nutritional anaemia of infancy to pregnancy anaemia in the mother.

One would be justified to conclude, therefore, that the presence of anaemia in pregnancy reduces the margin of safety for the mother and her foetus. Hence it is important to detect this anaemia as early as possible. Yet in pregnancy the clinical features of anaemia are liable to be overlooked very easily, because the usual signs and symptoms are obscured by the effects of pregnancy (Davidson, 1951, p. 147; Gatenby and Lillie, 1955; Fisher and Biggs, 1955). The onset is insidious. Dyspnoea is common, but it is seldom rightfully ascribed to the presence of anaemia. Other complaints that tend to occur without arousing suspicion of anaemia are anorexia, malaise, pallor, ankle oedema, palpitations, epigastric discomfort and bowel irregularity. As a matter of fact, it has been repeatedly calculated that anaemia can pass unnoticed in pregnancy in about 50 per cent of cases. The clinical features become unequivocal only when the haemoglobin level falls to or below 6 g. per 100 ml. of blood (Gatenby and Lillie, 1955; Tasker *et al.*, 1956). Clinical judgment is certainly too fallacious in deciding on the presence or absence of anaemia in pregnant women.

There remains no doubt that haemoglobin estimation in pregnancy is essential. This is the universal consensus of opinion, as evinced in most textbooks of midwifery. Whitby (1932) was among the first to advocate this practice. Greenhill (1951) and Davidson (1951, p. 147) recommend haemoglobin estimation as an important routine screening test at about the 36th week of pregnancy. At this late stage, however, it may prove difficult to institute adequate anti-anaemic treatment in some cases. It may also be irksome to the patient. A haemoglobin estimation at about the end of the first trimester (Rath *et al.*, 1950; Browne and Browne, 1955, p. 462) is equally desirable. Consequently Klopper and Ventura (1951), Israëls (1955), and Gatenby and Lillie (1955) consider that every pregnant woman should have her haemoglobin estimated on two occasions, viz., at her first attendance (usually at 10 to 16 weeks) and again a few weeks before term. These readings constitute the bare minimum. Rath (1950) and Dieckmann (1952) prefer the haematocrit; Lund (1954) regards it as one of the most accurate and valuable single tests, though Berlin and co-workers (1953) find it "grossly inadequate" for the total volume of red cells. At the same time Holly (1953) has pointed out that mere determination of the haemoglobin level, erythrocyte count and colour index does not always suffice to unmask iron-deficiency, for the iron reserves may be severely depleted before the blood findings are appreciably affected.

A limit must be defined for the blood levels below which the condition be termed anaemia. It has been customary to regard the physiological limits in pregnancy, particularly in the second and third trimesters, to be at a lower level than in non-pregnant women. The minimal figures usually quoted are those originally propounded by Adair, Dieckmann and Grant (1936): haemoglobin 10 g. per 100 ml., red blood corpuscles 3,360,000 per c.mm., and packed cell volume 33 per cent. There is a growing tendency, however, to question the "normality" of these figures. Thus, Holly (1955) believes that the commonly accepted standard of 10 g. of haemoglobin per 100 ml. of blood is much too low: he asserts that pregnant patients with a haemoglobin level less than 12 g. are likely to have a deficiency of iron.

This telling discrepancy cannot be allowed to go on. It is imperative to decide what the minimal standards should be for these blood values during pregnancy, especially in view of the dangers already outlined. Osten (1953) insists that in all haematological work the figures for the haemoglobin level and for the number of red and white blood corpuscles can only possess practical and diagnostic value if they be considered in relation to the blood volume. And it is precisely because in pregnancy there is an increase in the blood volume causing a dilution of the corpuscles that the convention arose to lower these normal standards: the condition has been described as a relative anaemia due to blood-dilution or hydraemia.

Several studies have been published on this hydraemia of pregnancy, a notable feature of these papers being the discrepancy in the results reported. This discrepancy has been accentuated with the use of more modern methods for the calculation of blood and plasma volumes. The earlier estimations made use of dyes, and the observed increase of the blood volume during pregnancy was highly inconsistent in incidence and in amount. In Germany Schultz (1933) examined 567 pregnant women, of whom only 50 per cent showed any hydraemia. The earlier observations were well reviewed by Dieckmann and Wegner (1934) who deduced therefrom an average increase in the blood volume ranging between 10 and 20 per cent. In their own experiments, several cases showed no increase and some even a decrease; the average increment in the plasma volume being 40 per cent and in the total blood volume 23 per cent, while the red cell volume increased only by an average of 20 per cent. Strauss (1934) drew a clear distinction between hydraemia and hypochromic anaemia as they occur in pregnancy. This discrimination was reiterated by Boycott (1936), who sought to explain his group of patients with low haemoglobin levels and normal colour indices on the basis that the increase in the plasma volume was causing a dilution of the red cells; he reported the maximum degree of hydraemia to occur at the thirty-second week of pregnancy. On the other hand, Roscoe and Donaldson (1946) noticed a steady increase in the blood volume throughout pregnancy, but again there were "large variations" in the amount of this increase. Wolff and Limarzi (1945) imply that hydraemia does not begin to set in before the third and fourth month. Wintrobe (1951, p. 280) states that at term the increase in plasma volume may amount to 40 per cent and the increment in the total blood volume may be 32 per cent or greater. Yet Adams (1954), using a newer method, finds that the maximum rise in plasma volume amounts to 22 per cent; this level is reached at 32 to 34 weeks and does not decrease significantly in the last trimester. These findings again are not borne out by those of Gemzell, Robbe and Sjöstrand (1954), who report that the average increase in blood volume is 30 per cent, that the main rise occurs in the first half of pregnancy, and that there is a small decrease during the last four weeks. Caton and co-workers (1949) demonstrate an even greater fall in the plasma volume occurring shortly before the onset of labour: this diminution amounting to as much as 25 per cent.

It is evident that the incidence and degree of hydraemia in pregnancy are not constant. Dilution of the blood occurs in a varying proportion of pregnant patients and in varying amounts. It may begin early in pregnancy or at the third or fourth month. Its peak may be reached at 32 weeks or even towards term, but as the onset of labour approaches a slight to marked reduction in this hydraemia may occur.

More detailed attention is being paid in recent years to the fundamental changes occurring in the blood during pregnancy in order to obviate any misrepresentations that may be caused by blood dilution (Fay, Cartwright and Wintrobe, 1949; Ventura and Klopper, 1951; Hamilton, Higgins and Alsop, 1954). Thus, apart from assessing the fall in the level of haemoglobin per unit volume of blood, attempts have also been made to estimate the total amount of circulating haemoglobin: the results have been disappointingly contradictory, some authors reporting no substantial alteration (Ventura and Klopper, 1951), others an absolute increase (Dieckmann, 1952). Agreement is, however, reached on the viewpoint that the total number of erythrocytes increases progressively though at a slower rate than the plasma volume. The haematocrit value is reduced; the fall, however, is not uniform in view of the inconsistent fluctuations in the plasma and cellular components. It follows that greater reliance should be placed on the mean corpuscular haemoglobin concentration (Whitby and Britton, 1953; Simpson, 1954); Wolff and Limarzi (1945) state that it "tends towards normal values" in cases of hydraemia in pregnancy, and Israëls (1955) believes that a figure below 30 per cent indicates iron-deficiency anaemia. The serum iron level has persistently been found to be reduced, especially from the twentieth week onwards; and the same can be said for a rise in the unsaturated iron-binding capacity of serum proteins. There is also a significant

increase in the level of serum copper appearing before any change in the level of serum iron. The few estimates that have been made on free protoporphyrin values have yielded inconstant results, namely, no change, a slight rise, or a definite increase. Studies of the bone marrow have shown no alteration in the erythroid series but the leucocytic picture indicates hyperplasia, especially in the later months.

In the face of this array of data, it is indeed surprising that hydraemia in pregnancy should still be regarded as a physiological phenomenon. It is often argued that several advantages accrue from this increase in the blood volume, the one usually cited being that the hydraemia is an insurance against blood loss at the time of parturition (Clayton, 1951; Wintrobe, 1951, p. 280). However, this alleged advantage can easily be shown not to hold true. There is, in my opinion, every evidence to indicate that hydraemia is not a physiological event in pregnancy. Several arguments can be marshalled in support of this conviction.

Attention has already been drawn to the observation that in the last few days or weeks of pregnancy a diminution occurs in the hydraemia (possibly by as much as 25 per cent). This certainly does not lend support to the contention that the main physiological purpose for blood dilution is the saving of blood during labour. Had that been the case, a still greater increase in the hydraemia would have been expected at the approach of term.

Secondly, the augmented blood volume unduly adds to the burden on the maternal and foetal hearts—definitely not a physiological gain. Stander, Duncan and Sisson (1926) studied the circulatory changes in the pregnant dog, and they concluded that the minute volume of the heart rises by 30 to 50 per cent. Adams (1954), using a newer technique, found that the cardiac output reaches a peak at 28 weeks, when it is 32 per cent above the levels in non-pregnant controls; the non-pregnant level is again reached at 38 to 40 weeks. It is interesting to note that these findings coincide with the relevant variations observed in the hydraemia of pregnancy. According to Browne and Browne (1955, p. 436) several reliable estimates have shown that the minute volume increases steadily till about the 37th week, when it may be as much as 60 per cent greater than before the onset of pregnancy. It is logical to assume that the minute volume of the maternal heart must increase at least in proportion to the increment in the total circulating volume of the blood brought about by the hydraemia. Moreover, the greater the relative dilution, the less is there oxygen per unit volume of blood, hence the quicker must the cardiac output be in order to cope adequately with the metabolic needs of the body. At the same time, it is to be recalled that there is a rise in metaboljsm caused by the additional foetal, uterine and other general requirements. To meet these demands the presence of hydraemia is of no help. The foetus, too, suffers a bigger hardship as a result of blood dilution in the mother. Barcroft (1947) records that direct cardiometric studies on the foetus of the sheep show a rise in the output of the heart as the foetus grows older, though again there is probably a fall in the last two or three weeks of pregnancy. He also points out that this relatively enormous burden placed upon the foetal heart is in part the price exacted by a system of respiratory exchange so inefficient as that of the placenta. With the distinctive properties of foetal haemoglobin, the foetus is enabled to overcome the twin disadvantages of a poorly permeable diffusion membrane in the placenta and of comparatively low oxygen pressures in the maternal sinuses (Wright, 1956). Hydraemia, on the contrary, with its consequent reduction in the oxygen-carrying power per unit volume of maternal blood, only adds further to these respiratory difficulties of the foetus.

A third point against the concept of physiological hydraemia in pregnancy is the fact that it is far from being a universal or constant finding. This inconsistency has already been stressed above. It is an elementary principle of physiology that inconsistency can hardly be a feature of normality.

Berlin and co-workers (1953) have carried out a study on the blood in pregnancy by the use of P^{32} labelled red corpuscles. Their data show an initial drop in the total red cell volume early in pregnancy, and this is taken by them for an indication that there is a true anaemia in the first and second trimesters and that the decrease

in the red cell count and haemoglobin is not entirely due to hydraemia. This decrease, I consider, can hardly be due to hydraemia. As we have already seen, there is no demonstrable blood dilution occurring in the first trimester. Any anaemia in this period could not, therefore, be ascribed to a causal hydraemia.

This important point of not allowing the concept of hydraemia to mask or belittle the presence of anaemia is again brought into relief on consideration of the post-partum changes. Lowenstein, Pick and Philpott (1950) have found that the fall in the blood volume from the immediate ante-partum period to the immediate post-partum period amounts to an average of 1,200 ml. A degree of anaemia, however, persists. Young and co-workers (1946) have therefore pointed out that, since it appears likely that after delivery the blood volume returns to normal fairly quickly without a corresponding improvement in the anaemia, a certain amount of iron deficiency is postulated.

Considerable emphasis must also be laid (because it seems to have largely escaped attention) on the very close resemblance between the features of the so-called physiological hydraemia of pregnancy and those of a simple iron-deficiency anaemia. This similarity is brought out in several published papers, notably those of Fay *et al.* (1949), Lundström (1950), and Ventura and Klopper (1951). An iron-deficiency state is characterized by a fall in the serum iron; not only does such a fall occur in pregnancy hydraemia, but it is greater than would be expected from the dilution effect of the hydraemia. In iron-deficiency anaemias the iron-binding capacity of the blood is raised (Laurell, 1947). A similar rise occurs in pregnancy in spite of the hydraemia, the total iron-binding capacity increasing against the gradient of dilution. This rise has been found to be even higher than can be explained on the basis of the fall in serum iron. There may also be an increase in the level of free protoporphyrins during pregnancy, a change compatible with a condition of iron lack. The hydraemia itself finds a correlation in anaemic states: it has been established (Gibson, 1939; Whitby, 1949) that the plasma volume in untreated anaemia is usually greater than in normal subjects, and that during treatment this volume falls gradually to normal as the red cell count rises. Increased iron absorption has been observed by Copp and Greenberg (1946) to be a feature of iron deficiency states in general; hence it is interesting that Balfour *et al.* (1942) and Darby and co-workers (1955) have shown iron absorption to be progressively increased in pregnancy. Similarly, achlorhydria has been repeatedly reported in pregnancy (vide infra); and in a study of the gastric mucosa in hypochromic anaemias Davidson and Markson (1955) arrive at the suggestion that it is after iron-deficiency anaemia has become established that achlorhydria develops. It is also of interest that Davies and Shelley (1934) observed that the gastric secretion was usually normal in women who showed no anaemia during pregnancy. This multiplicity of features in common between hydraemia of pregnancy and iron-deficiency anaemia is inevitably impressive.

A final argument against the tenet that hydraemia is a physiological occurrence in pregnancy is found in the fact that the low haemoglobin level is invariably amenable to iron therapy. This point is considered later; here it is worth pointing out that even when there is gross anaemia adequate treatment is liable to raise the haemoglobin level well above the "physiological" standard of 10 g. per 100 ml. as hitherto accepted.

The borderline between physiology and pathology is often difficult to define. Enough has been said, however, to challenge, if not invalidate, the postulate of a low haemoglobin level being ever explicable on the basis of physiological anaemia or hydraemia. Moreover, the picture of hydraemia in pregnancy runs parallel to several other pathological conditions.

One of these analogous conditions is the anaemia occurring in renal disease when nitrogen retention has developed (Wintrobe, 1951, p. 548). The suggestion was made that the anaemia of chronic nitrogen retention was due to increased plasma volume or hydraemia. This is no longer held, though the cause of the anaemia has not been clearly defined. Any one or more of such factors as inhibitory toxins, faulty diet, defective absorption, or a deficiency in haemoglobin metabolism, may play a role in

individual cases. Almost an identical state of affairs, together with the same hydraemia, obtains in pregnancy. Another striking similarity is the decrease in gastric acidity observed in chronic glomerulonephritis as anaemia becomes more marked.

Hydraemia has also been assailed in its alleged role of bringing about other changes in the blood. There is a fall in the level of plasma proteins during pregnancy (Canterow and Trumper, 1949), the diminution occurring mainly or entirely in the albumin fraction. This decrease is often attributed to the hydraemia. However, Melnick (1937) regards the synthesis of body protein in the foetus as a form of internal plasmapheresis leading to depletion of the maternal serum proteins. He believes that these parasitic effects on the maternal organism are of primary importance, over and above the factor of hydraemia, in causing the characteristic decrease in serum protein concentration during pregnancy.

We are thus inevitably drawing towards the conclusion that hydraemia in pregnancy is merely part of a deficiency state. There may be concomitant deficiency of protein as well as deficiency of iron, with resultant low blood levels of haemoglobin and, to a less extent, of red cells. It is, in fact, not sufficiently realized that pregnant women are on the verge of iron-deficiency anaemia.

In general, it is often only the iron stores of the body that limit a would-be condition of manifest anaemia to one of latent deficiency. The body stores in a healthy adult range from 1·0 to 1·5 g., while the amount of iron in the circulating haemoglobin is between 3 and 3·5 g. This extra gramme or so may become all-important whenever there is a tendency for the haemoglobin level to fall. If, however, such a tendency persists for any length of time, the iron stores become depleted, and no safeguard remains against the development or deterioration of an anaemic state. Suffice it to remember that the dietary intake of iron may easily fail to balance the daily excretion of this mineral. Thus, the average absorption of iron from food is between 1·0 and 1·5 mg. daily. It may be greater in patients with iron deficiency. On the opposite scale of the balance, Moore (1955) has calculated the excretion of iron in desquamated skin-cells, sweat and urine to be about 1 mg. daily. Hence the gain is meagre.

The position becomes more precarious when women are considered. Fullerton (1936) found the diets of poor women in Aberdeen very frequently inadequate to compensate for the iron demands in reproductive life, i.e., menstruation and pregnancy. Menstruation, for example, entails a further monthly loss of 14 to 28 mg. of iron. Over a 28-day cycle, this corresponds to an average daily loss of 0·5 to 1·0 mg. No wonder that Fullerton observed the incidence of anaemia to be very high in women of the poorer classes.

In pregnancy the balance of iron metabolism is even worse. In a series of papers Davidson and Fullerton (1938) showed that the saving of iron due to the absence of menstruation failed to counterbalance the increased demands during pregnancy. These extra requirements are represented by the sum of 400 mg. for the foetus and 150 mg. for the placenta and hypertrophied uterus. If this total of 550 mg. (at least twice the amount saved from menstruation) is considered to be built up over the whole period of 40-weeks gestation, the daily demand works out to just under 2 mg. An even higher estimate of the total iron loss during pregnancy was reached by Hamilton, Higgins and Alsop (1953). One is consequently disturbed by the findings of Hamilton, Higgins and Alsop (1954), who report that the maximum absorption of iron during pregnancy from a normal diet is only 1 mg. daily. The gravid mother, however, has been shown to require an average of 3 mg. More detailed study of these iron demands reveals the main danger to lie towards the end of pregnancy. Browne (1947) points out that in the last two months the iron content of the foetus increases from 80 to 400 mg., which amounts to a storage of no less than 5 mg. daily. Rath *et al.* (1950) have analyzed further the daily needs for iron by the mother as they increase throughout pregnancy. They conclude that about 1 mg. a day is required during the first trimester, 4 mg. a day during the second trimester, and as much as 10 to 12 mg. a day during the latter part of the third trimester. In view of all this, little doubt remains that the

average pregnant woman is on the brink of iron deficiency, latent or manifest.

Added to this risk is the problem of hypochlorhydria in pregnancy with its consequent impairment of iron absorption. Nakai (1925) observed that in his 14 pregnant patients the gastric acidity was lower than the level reported by other Japanese workers in non-pregnant women. Arzt (1926) confirmed this hypochlorhydria in 18 women. Strauss and Castle (1932) found that 75 per cent of their patients had hypochlorhydria or even achlorhydria throughout their pregnancies, the gastric acidity returning to normal in the puerperium. The temporary nature of this reduction in gastric acidity was verified by Davies and Shelley (1934), who further noticed that women showing this hypochlorhydria were apt to develop hypochromic anaemia during or after pregnancy. In their opinion this anaemia was a consequence of the impaired acid secretion of the stomach. On the other hand, Clark and Tankel (1954) made repeated estimations of the gastric acidity in 9 gravid women but they failed to corroborate the occurrence of hypochlorhydria in pregnancy. In their paper, however, no mention is made of the possible relation of gastric acidity to the blood picture.

In pregnancy, then, anaemia is no mere bugbear. In other words, a low haemoglobin value should not be simply ascribed to hydraemia and left untreated. It demands vigorous iron therapy in all cases. Several reports have been published in the last six years proving the efficacy of iron treatment in cases which would otherwise have been neglected on the grounds of physiological hydraemia of pregnancy. Magee and Milligan (1951) found that women having iron had higher haemoglobin levels after labour than women not having iron, the effects of this treatment being more pronounced the longer the iron was taken. Davidson (1951b) in a personal observation claimed that with effective iron therapy the haemoglobin would rise above the "physiological level" to 90 per cent (13·3 g.) or higher. Benstead and Theobald (1952) showed that the administration of iron from the 24th week caused a rapid recovery from the commencing "physiological" anaemia, and that thereafter satisfactory normal blood values were maintained throughout pregnancy. It is pertinent to note that they observed similar improvements in the mean corpuscular haemoglobin concentrations. The efficacy of iron therapy in raising the haemoglobin level from an initial range of 10 to 13 g. per 100 ml. to within the normal non-pregnant range has also been demonstrated by Davis and Jennison (1954). There have been several other papers recording a rise of the haemoglobin level in pregnancy to 12 g. or more as a result of treatment with iron (Hamilton *et al.*, 1954; Gatenby and Lillie, 1955). This rise may even be sharp according to Fisher and Biggs (1955).

An apparent failure in treatment is reported in some earlier papers. Thus, Adair, Dieckmann and Grant (1936) stated that iron administered during pregnancy failed to maintain the normal level of haemoglobin. This opinion is repeated by Roscoe and Donaldson (1946), iron therapy not raising the haemoglobin level unless the colour index was low. More recently Berlin *et al.* (1953) have suggested that supplemental oral iron has little or no effect on the total red cell volume in normal pregnancy. That some cases do not respond satisfactorily to iron therapy by the oral route is readily understood. However, on reviewing the recent literature, the conclusion is reached that modern methods can correct most, if not all, cases of anaemia in pregnancy—irrespective of the underlying fault in iron metabolism. It is important to keep in mind the possible reasons for failure. One tends, for instance, to forget that many pregnant women cannot tolerate ferrous sulphate pills and so they do not take them. Another point is that of inadequate dosage or duration of treatment: here lies the blame in most cases of failure of oral iron therapy. Defective absorption has also to be reckoned with; thus, Hamilton *et al.* (1953) found the addition of ascorbic acid or dilute hydrochloric acid to be often effective in cases with an unsatisfactory response. In some cases it may be necessary to administer iron by the parenteral route, either intravenously (Klopper and Ventura, 1951) or intramuscularly (Jennison and Ellis, 1954). These authors point out that by means of the parenteral route all faults in the mechanism of iron metabolism below the level of utilization

are short-circuited: success being achieved in the urgent treatment of anaemia detected late in pregnancy as well as in cases due to dietary shortcoming, a breakdown in iron absorption, or depleted iron reserves. On the question of iron reserves, Bradshaw (1956) quotes Haskins *et al.* (1952) as demonstrating that even six-months administration of oral iron may have no effect on depleted stores. Bradshaw recalls that, as the haemoglobin level rises with treatment, so does the intestinal mucosal block to iron absorption become more effective, the consequent danger being run of failing to build up the lost iron stores as rapidly as required. Hence in these instances parenteral iron therapy is indicated. Above all, it is evident that today no case of anaemia in pregnancy should ever be conceded as being refractory to treatment.

Since anaemia in pregnancy is so readily curable and since all pregnant women exhibit a serious tendency to anaemia, there is every reason to raise a plea for the routine administration of iron during pregnancy. This is no solitary appeal. From their findings Fisher and Biggs (1955) conclude that it is advisable to prescribe iron for all pregnant women and to see that it is really taken. This practice is emphasized by Lundström (1950). That it should at least be done in the last trimester of every pregnancy is called for by Holly (1955) and by Gatenby and Lillie (1955). Further, Hamilton *et al.* (1954) consider that, to be truly effective, iron must be administered for 150 days before delivery is expected. This observation that better results are obtained if iron is started before the 20th week is confirmed by Scott (1956), who points out that, if hydraemia is allowed to set in, the rise in haemoglobin may be considerably reduced. Much, therefore, can be said in favour of routine iron administration during pregnancy, especially from the third or fourth month to term. At hospital antenatal clinics, where the haemoglobin level is checked as often as necessary, such a practice may perhaps be partially waived. But these clinics are attended by only a minority of pregnant mothers. It is on the general practitioner and on the midwife that the responsibility falls not merely for the detection and treatment of anaemia in pregnancy, but even more so for its prevention. And certainly there is no more effective method than the routine administration advocated.

Conclusions

For several reasons hydraemia in pregnancy should no longer be regarded as physiological. Low levels of haemoglobin are not primarily attributable to the hydraemia. The pregnant woman is already in a precarious position of iron deficiency, latent if not manifest. She is also liable to show a negative balance of protein—perhaps of other essential food constituents as well.

Hydraemia is one of the manifestations of this deficiency state in pregnancy. As hinted by Benstead and Theobald (1952), it is worth investigating whether the incidence and degree of hydraemia in pregnancy could be significantly reduced by ensuring adequate body stores and blood levels of iron and proteins, in the same way that the increased plasma volume of a simple iron-deficiency anaemia can be diminished with effective iron therapy.

The term "physiological anaemia of pregnancy" should be discarded once and for all. The minimum haemoglobin standard for pregnant patients should henceforth be taken as 12 g. per 100 ml. blood (Hamilton *et al.*, 1954; Holly, 1955; Cope *et al.*, 1956). With a haemoglobin reading below this level patients should be considered to be anaemic, and effective iron therapy instituted at once.

The relation of hormones to hydraemia in pregnancy has not been discussed. Such hormones as pituitrin, adrenocorticotrophic hormone, cortisone, and progesterone probably play an important role in this connexion. It is possible that the endocrine changes occurring during pregnancy may profoundly influence the bone marrow (Berlin *et al.*, 1953) and the plasma volume. If, for instance, the mechanism for the production of hydraemia were shown to be mediated through progesterone, then the hitherto unexplained diminution in the hydraemia at the approach of term would be accounted for by the fall in the level of progesterone caused by the normal stimulus for the termination of pregnancy.

Further research into the relation of gastric acidity to anaemia in pregnancy may also prove

profitable. When heartburn in the early months is due to hyperacidity, it is worth investigating whether this could be a physiological response to the need for more effective absorption of iron. Conversely, with adequate prevention of anaemia in pregnancy, the incidence of hypochlorhydria and achlorhydria may well fall (cf. Davidson and Markson, 1955).

Summary

It is essential to define reliable standards of anaemia in pregnancy in order not to neglect patients who require treatment. This point is illustrated in a limited investigation.

The dangers of this anaemia—to the mother and, to a less extent, to her baby—are outlined. It is emphasized that the clinical features may be missed very easily, unless the haemoglobin level falls below 6 g. per 100 ml. The haemoglobin should, therefore, be estimated routinely in pregnancy, at least twice.

Anaemia in pregnancy has been alleged to be often the result of increase in plasma volume. A review is given of the incidence and laboratory features of this hydraemia. Reasons are adduced for the belief that hydraemia is not a physiological event in pregnancy.

Pregnant women are shown to verge on iron-deficiency anaemia. Increase in plasma volume is postulated as part of the picture of a deficiency state in pregnancy. The anaemia can invariably be corrected with adequate iron therapy. A haemoglobin level less than 12 g. per 100 ml. in pregnant women should be considered as abnormal.

An appeal is made for the routine administration of iron during pregnancy, particularly in domiciliary practice.

Some new observations are made, and further research along certain lines is suggested.

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A HYSTEROGRAPHIC STUDY OF UTERI AFTER CAESAREAN SECTION

BY

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THE problem concerning the mode of delivery subsequent to Caesarean section is a real one. There is little scientific evidence available on which to base a sound decision; and much has yet to be learnt before we gain a rational approach to this serious matter. The possibility of gaining some further knowledge of the actual scar area from an X-ray study stimulated this work.

There is no measure of efficiency of uterine scars save that of subsequent experience and even this may be misleading for there are those women who have reserved their rupture until perhaps the second, or even later, vaginal delivery following a Caesarean section.

The validity of the statement "Once a Caesarean section always a Caesarean section" is still very seriously "sub judice". Many studies of a clinical and histological nature have as yet failed to provide the truth.

To illustrate the divergence of world opinion, Bak and Hayden (1955), after studying 52 cases of uterine rupture in 71,483 deliveries at the Chicago Lying-In Hospital, state, quite firmly, that they believe "Once a Caesarean section always a Caesarean section".

Wilson (1951), after reviewing this question in the Department of Obstetrics and Gynecology, Cornell University Medical College and the Women's Clinic of the New York Hospital, stresses individual management with a considered opinion in each case. He points out that if all cases were scheduled for repeat sections there would still be a few spontaneous ruptures prior to this time.

Donald Fraser (1953) adequately expressed the view that repeat Caesarean section is far from being the accepted rule or practice in Britain. Birnbaum (1956) states that, in the New York Lying-In Hospital, repeat Caesarean section is the rule on the private service and vaginal delivery is aimed at in the ward service.

In the two obstetric teaching hospitals of Adelaide, the Queen Victoria Maternity Hospital and the Queen Elizabeth Hospital, Maternity Section, there has been no case of rupture of the uterus following Caesarean section in the last 5 years. During this period of over 17,000 deliveries, 216 women presented giving a history of previous Caesarean section delivery. Eighty-three of these were conducted safely through a vaginal delivery, the other 133 had repeat Caesarean section, a large proportion having a recurring indication. Our policy is one of individual selection after a full consideration of the reason for the previous Caesarean section, age, pelvis, uterine action, convalescence, history of the present pregnancy and any other relevant information.

Most would agree that once a Caesarean section has been done on behalf of a genuinely recurring indication such as pelvic contraction then the subsequent decision in favour of repeat Caesarean section is easy. What of the non-recurring indications? The well-worn and unreliable clinical criteria usually quoted, on

which to base a decision, are, firstly, the presence or absence of a pyrexial convalescence often without any real regard for the possibility of pyrexia from other causes than the operation site. There is much evidence to show that sound uterine wound healing can occur in the presence of pyrexia. Secondly, abdominal wall wound-healing cannot always be directly related to uterine wound healing. Again tenderness and pain over the uterine scar is unreliable as an indication of impending rupture as shown by Cosgrove (1951). Vaginal bleeding during the first stage of labour has been regarded as an important warning sign of rupture or impending rupture of the uterus but personally this has been found unreliable on many occasions. Haematuria would be expected in rupture of the lower segment scar if the bladder were involved in the scar area, but this is a sign which, of necessity, can only be present when actual rupture has occurred; it is not likely to help the decision before labour. Information regarding the technique and skill of the previous operator, within reasonable limits, has also been found prognostically unreliable.

Most obstetricians have grown to accept the greater safety of the lower segment operation and this view has been supported statistically in many papers. Recently, however, Lane and Reid (1953) have expressed their doubts even of this thesis. After examining their results in Boston they reported a 3·3 per cent incidence of wound rupture in the lower uterine segment as against a 1·3 per cent incidence of rupture subsequent to classical Caesarean section. The vertical incision in the lower uterine segment was used mostly in this material and it is quite possible that this may be responsible for the high incidence of dehiscences in their lower segments.

Dewhurst (1957) has produced the most recent British paper in which he supports the majority opinion on this question and shows a 2·2 per cent incidence of rupture in classical scars and a 0·5 per cent from lower uterine segment scars. The maternal mortality in his series was 5 per cent from 100 cases of classical rupture, none dying from 55 ruptures of the lower segment. The foetal mortality was 73 per cent from the former as against 12·5 per cent from the latter.

These papers are but examples of many which provide widely divergent views and, although there would appear to be many reasons for this, it is not our intention to pursue this question further here.

Previous Investigations

The histological studies of Schwarz *et al.* (1938) and Siegel (1952) show conclusively that original healing of wounds in the uterus takes place by fibroblastic reaction producing a fibrous tissue union. Later this area of fibrous tissue union shrinks and is even absorbed into the surrounding muscle so that later the union may appear to be by direct muscle to muscle union.

Baker (1955) published the only paper we have been able to find on such a hysterographic study of the uterus following Caesarean section. He manually examined the interior of the uterus of 64 patients who had vaginal deliveries following previous lower segment operations and reported 53 as having a sound scar. In 24 of his 64 patients he obtained hysterograms about 3 months after the vaginal delivery. He was able to demonstrate a deformity in the lower anterior wall of the uterus in only 5 cases out of 24. Our own experience of manual exploration of a previously sectioned uterus immediately following a vaginal delivery has been rather inconclusive. The soft and flabby state of this lower segment area at this time makes firm conviction regarding an intact scar very doubtful. Our study therefore concentrated entirely upon the X-ray appearance of uteri which had been sectioned. With our technique, emphasizing the lateral view, we have been able to demonstrate a deformity in every uterus which had been subjected to Caesarean section.

The Study

This study concerns patients who had been delivered in 1952 or subsequently at the Queen Victoria Maternity Hospital. It includes 13 women who had vaginal deliveries and 43 women who had Caesarean section delivery. This group of 43 is further subdivided into those who had one Caesarean section (26), those who had more than one Caesarean section (10), those who had a vaginal delivery subsequent to the Caesarean section (5) and those

who had a delivery following the hysterogram (2). All these women attended the Q.V.M.H. although not all the Caesarean sections had been done in that institution, there being a few who had Caesarean sections prior to 1952 but had subsequent deliveries at the Q.V.M.H. The time-interval between the Caesarean section and the hysterogram has exceeded 6 months in the majority of cases.

Those women who were the subjects of this investigation volunteered willingly, the hysterograms were mostly done in the early phase of the menstrual cycle, and there was no morbidity. At the interview a full obstetric history was obtained, the details of the examination were then explained to each woman, this was followed by an aseptic vaginal examination and then the hysterograms were taken. The technique was improved as the study progressed until finally best results were obtained using, in all, 7 millilitres of a viscous iodized oil. Some X-rays could not be interpreted and these have been grouped separately.

Technical Details

The interpretation of results has been based mainly on the lateral position film. The aim was to just fill the cervical canal and uterine cavity thus excluding the Fallopian tubes. No premedication was used and the woman was placed in the left lateral position on the X-ray table with the central ray passing through the femoral heads. The thighs were flexed and a pillow placed between her knees. A bivalve vaginal speculum was then inserted, with all aseptic precautions, and the anterior lip of the cervix gently grasped with a tenaculum. A screw-in metal cannula with a wide cervical head of the Leech Wilkinson type, previously filled with the contrast medium, was then used to procure a tight fit. A 10 ml. glass record syringe was then joined to the cannula using a thin-walled rubber tube and adaptor. Under direct vision 1·5 millilitres of Lipiodol Lafay, 40 per cent Iodized oil, was then injected to confirm free flow and absence of leakage. A protective lead shield with a small slit in its lower edge was next dropped into place for the protection of the operator, the cannula and tenaculum projecting through the slit. A further 4 millilitres were then slowly injected and as the last millilitre was being injected the exposure was made. The woman was then turned to the dorsal position with her legs extended, the cannula having been retained carefully in position in the cervix. With the protective screen repositioned a further 1·5 millilitres of Lipiodol was next injected and a second film taken whilst this was being done. It was found most important to continue injecting the media during the actual exposure. If this were not done the cervical canal and the lower part of the uterine cavity appeared to empty of media and were not shown on the film. Experimentation with the amount used was also necessary. Too little resulted in inadequate filling of the canal and lower part of the uterus and made interpretation difficult. Too much resulted in filling the Fallopian tubes and caused intra-peritoneal spilling which tended to obscure the scar site. Excessive amounts also caused ballooning-out of the cervical canal causing interpretation difficulties. High viscosity contrast media were found the best. Difficulty in the application of the screw-in cannula to a scarred and stenosed cervical os, or the too deep insertion of this cannula into a badly lacerated cervix, was overcome by the use of a Rubin type. The elongated tube-like tip of the Rubin's cannula in some cases tended to obscure the scar site.

The X-ray exposure details for the lateral position were KV 90; MA 200; Time 1 to 1·75 seconds, anode film distance 40 inches; Bucky ratio 8 to 1, Target area 2 mm. square; Du Pont "Patterson" Hi-speed thick screen.

The Results

A. Control Group—13 cases

Each case showed a regular smooth outline extending from the tip of the cannula well up into the lower half of the uterus (Fig. 1). Even in the retroverted uterus this typical appearance was constant (Fig. 2).

To demonstrate the anatomical features shown in these lateral hysterograms of the normal uterus a special composite picture was produced in the following way. With the patient in the lateral position on the X-ray table a uterine sound was introduced into the cervical canal until the resistance of the internal os was felt.

An exposure was then made. The sound was next removed and, without disturbing the position of the patient, the cannula was screwed into the cervical canal, Lipiodol injected and a further exposure made. These two developed films were then superimposed in exact anatomical register with the result shown in Figure 3. The area of slight constriction just above the tip of the sound represents the internal os. This same procedure was repeated on 3 further occasions with identical findings.

B. Caesarean Section Group—43 cases

Every uterus which had been subjected to a previous Caesarean section showed some degree of deformity. Not one of the 43 cases showed the typical smooth outline of the vaginal delivery group.

In an attempt to grade the deformities, each one has been measured in depth, the radiographic distortion factor being constant in all cases. An arbitrary division based on depth alone has been selected. Those deformities of 5 mm. depth or less have been graded as *small*, and those of 6 mm. or more have been graded as *large*.

(a) *Those cases who had one Caesarean section*—26 cases (2 not classified—see note*). Sixteen cases had small deformities and 8 cases showed large deformities. The commonest deformity was the small wedge-shaped projection (Fig. 4) and is the type detected in most of our cases. The large deformities have varied in size and shape from larger wedges to wide based sacculations (Figs. 5 and 6, lateral and A.P. views).

(b) *Those cases who had more than one Caesarean section*—10 cases (1 not classified—see note*). Eight cases had small deformities and 1 case showed a large deformity. In one case who had 2 Caesarean sections 2 separate defects can be seen (Fig. 7).

(c) *Those cases of vaginal delivery subsequent to the Caesarean section*—5 cases (2 not classified—see note*). One case showed a small deformity, another a large and a third, who had a classical Caesarean section, showed an extensive anterior uterine wall defect in a retroverted uterus (Fig. 8).

(d) *Those cases of delivery following hysterogram*—2 cases. One had a spontaneous uncomplicated vaginal delivery and she showed a small deformity. The second, whose X-ray also showed a small deformity (Fig. 9), was subjected to a repeat Caesarean section following an ineffective labour of 80 hours. At operation the site of the previous wound in the uterus was visible as a slightly thinner and paler tissue than the adjacent muscle.

To confirm the anatomical position of these deformities the procedure already outlined, using superimposed films, was used. The lateral film (Fig. 10) shows a typical irregular deformity with a wide base. The composite print (Fig. 11) shows the tip of the uterine sound touching the internal os.

In our endeavour to confirm that these deformities represented the Caesarean section scar one woman was subjected to hysteroscopy. This woman had 3 Caesarean sections and a tubal ligation with the third. A transverse scarred area was seen just above the level of the internal os. This was the expected finding after studying the X-ray (Fig. 12).

From 4 women who had previous Caesarean sections we obtained hysterectomy specimens. Each showed a well-marked external scar which corresponded with an internal deformity. Figure 13 shows one such uterus whilst Figure 14 shows a low power view of the scarred area.

We feel justified in concluding that these deformities thus demonstrated occur at the site of the uterine incision.

No relationship was detectable between the constant factor, the uterine deformity, and the many variables such as age, parity, indication for Caesarean section, time in labour, operative technique, post-operative pyrexia, wound healing or time of X-ray examination.

Discussion

The outstanding finding has been that all uteri previously subjected to Caesarean section showed some degree of deformity. The series is

* *Note.* There were 5 X-rays which we had difficulty in interpreting so we have not included them among the totals with definite deformities due to the Caesarean section. However we are certain that they are in no way comparable to those of the control group.

large enough for the elimination of chance. The 13 control cases showed such a constant regular outline of the lower uterine segment as to allow its acceptance as normal.

This X-ray study has given us more detail regarding the wound area than we had previously and it has served to expose the state of affairs which has, no doubt, been existent long before this study. In one sense, therefore, little of practical importance would appear to have been gained. On the other hand the detection of a sacculation, as shown in Figure 5 prior to the next pregnancy, may well be of great importance. No surer evidence of deficiency is needed than this. Deficiencies of this nature in the scarred area most likely represent a retrovesical pouching and we believe that, if detected, these women should certainly have a repeat Caesarean section. A uterus showing a minor degree of deformity should be allowed to have a natural delivery provided there are no other mitigating circumstances. We have no first hand experience of women with the major degrees of deformity—the sacculation type—going through subsequent vaginal deliveries; maybe even they could do it, with apparent clinical safety, although in our opinion it would be preferable to plan a repeat Caesarean section.

The practicability of submitting all women who have had Caesarean section deliveries to an X-ray investigation of the uterus is probably not regarded with enthusiasm, although a critical selection may eventually become quite practicable, and even indicated, in certain cases. This study has not been able to show that any clinical factor such as pyrexia, abdominal wall healing, surgical technique, etc., has been more prone to greater degrees of deformity so that it is not possible with any certainty to suggest the type of case which should be submitted to an X-ray examination. Further studies along these lines may do so. Nothing further than a broad statement such as "any case in which greater doubt than usual exists regarding the uterine wound healing should be selected for a hysterogram" is permissible at present.

The procedure has the advantage of being risk-free except in so far as it is an extra exposure to radiation which is another, yet potentially important, question.

Summary

(1) Fifty-six women have been the subject of a hysterographic study, 43 following Caesarean section and 13 normal vaginal deliveries for controls.

(2) Technical details are given in full.

(3) The 13 control cases all showed a smooth regular outline.

(4) The 43 cases following Caesarean section all showed some degree of deformity.

(5) The deformities have arbitrarily been divided into small and large depending on whether they were above or below 5 mm. in depth.

(6) Twenty-seven cases showed small scars, 11 cases showed large scars and 5 cases were not classified.

(7) No relationship has been shown to exist between the size of the deformity and the variable clinical factors such as age, parity, indication for Caesarean section, time in labour, operative technique, post-operative pyrexia, wound healing, or time of X-ray examination.

(8) It is advised that any case showing a large deformity should have a repeat Caesarean section.

(9) The practicability of X-ray examinations of the uterus after Caesarean section may be increased by selection of cases after further studies have been done.

(10) The procedure is safe.

Acknowledgments

We wish to thank Mr. I. B. Jose for conducting the hysteroscopy on one patient, and W. K. Nolan, Clinical Photographer, Royal Adelaide Hospital, and his assistant J. F. Guster, for their patience and care in the preparation of the photographs. Particular thanks are due to the members of the X-ray Staff of the Queen Victoria Maternity Hospital, especially C. W. Cook, the Radiographer, for his close co-operation and assistance.

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FIG. 1
Lateral hysterogram of normal anteverted uterus.

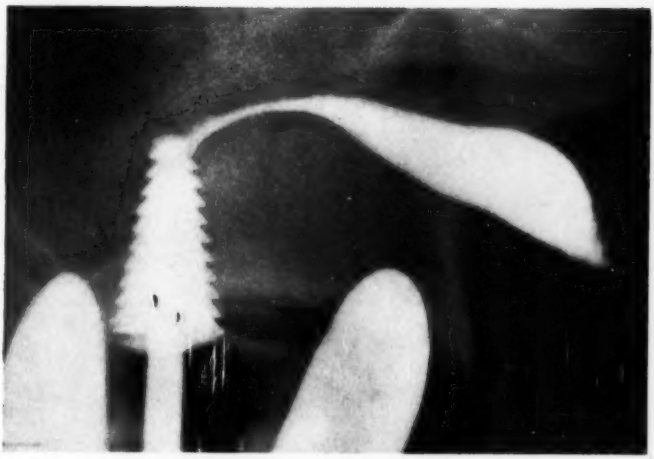

FIG. 2
Lateral hysterogram of normal retroverted uterus.

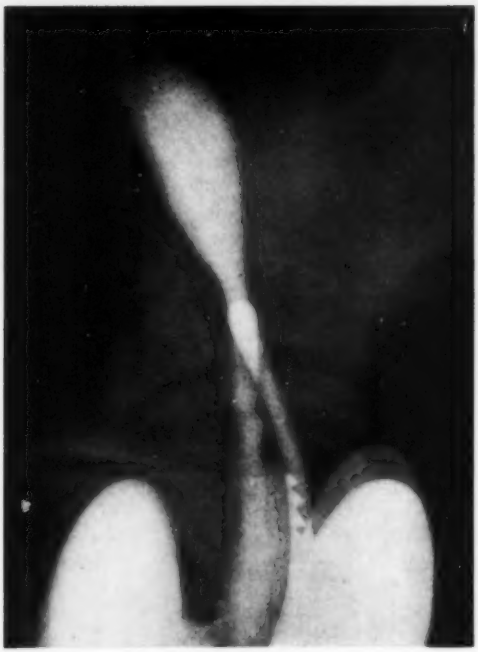

FIG. 3
Composite picture of normal uterus demonstrating site of internal cervical os.

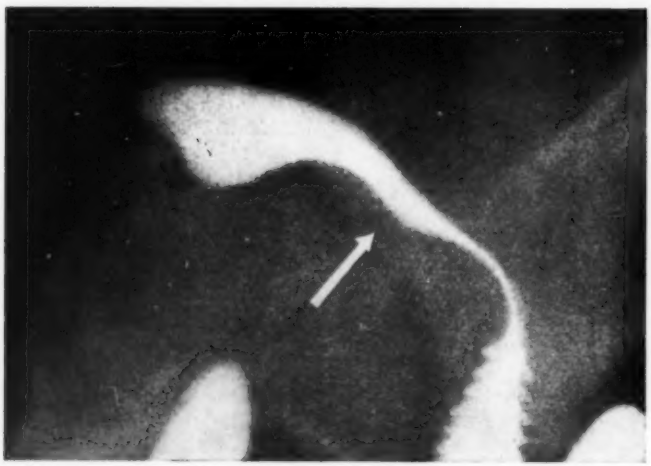

FIG. 4
Lateral hysterogram showing commonest deformity found after Caesarean section.

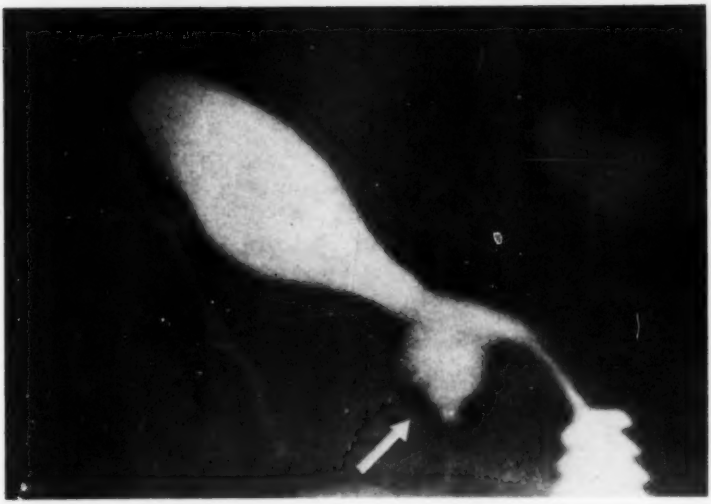

FIG. 5
Lateral hysterogram showing large deformity found after Caesarean section.

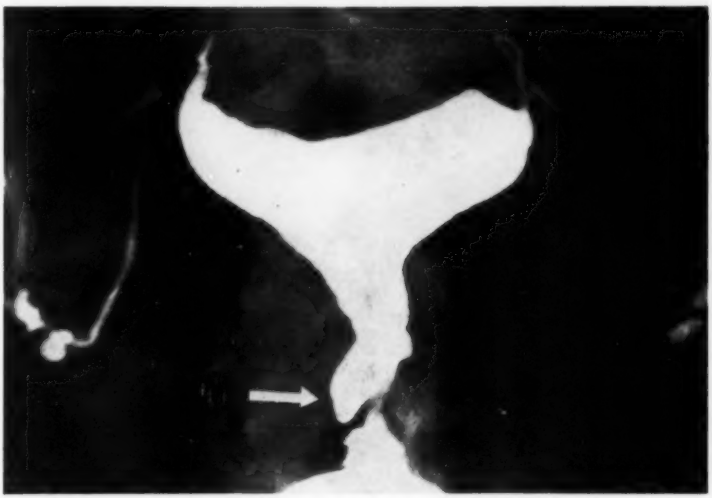

FIG. 6
Same case as Fig. 5 showing large deformity in A.P. view.

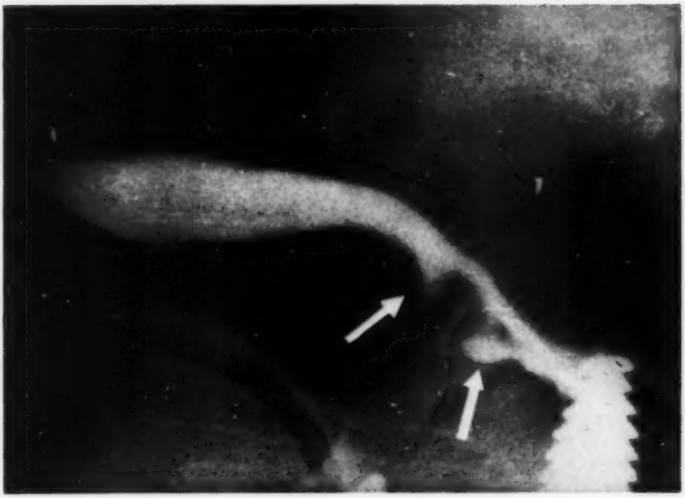

FIG. 7

Lateral hysterogram showing two separate defects in a uterus previously subjected to two Caesarean sections.

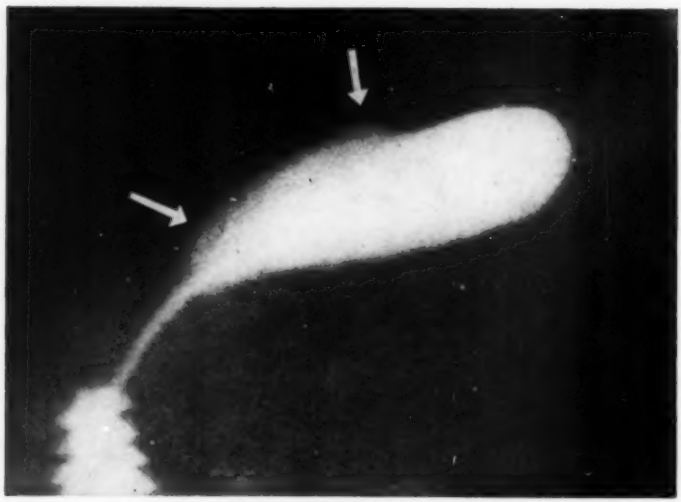

FIG. 8

Lateral hysterogram showing an extensive anterior wall defect in a retroverted uterus previously subjected to classical Caesarean section.

FIG. 9

Lateral hysterogram showing small deformity. Patient was subsequently delivered by repeat Caesarean section.

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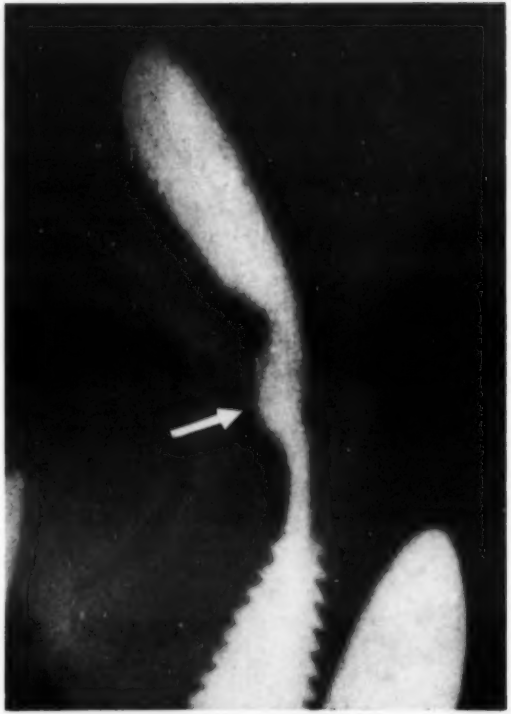

FIG. 10
Lateral hysterogram showing deformity found after Caesarean section.

FIG. 11
Composite picture of same case as Fig. 10 demonstrating site of internal cervical os.

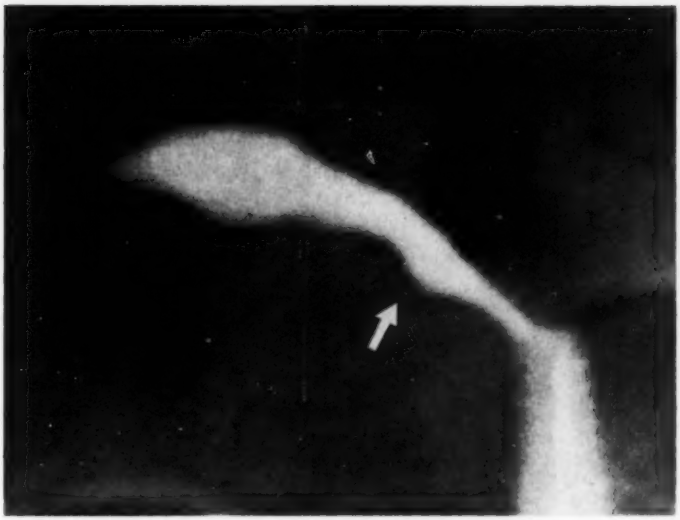

FIG. 12

Lateral hysterogram showing deformity found after Caesarean section in patient upon whom hysteroscopy was performed.

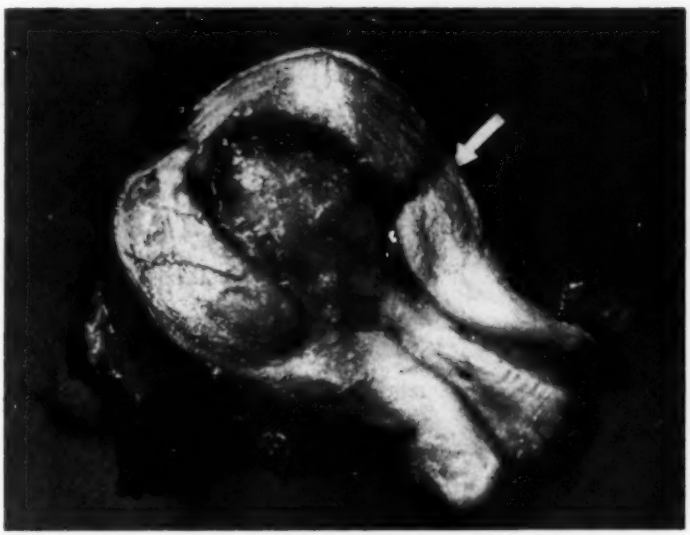

FIG. 13

Uterus opened in sagittal section. The arrow points to the site of the visible external scar of a previous Caesarean section.

FIG. 14
Section of scar area from same case as Fig. 13. ×5.

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THE NATURE OF PAGET'S DISEASE OF THE VULVA

A Study of Two Cases, One With and One Without Underlying Carcinoma

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PAGET'S disease of the vulva has only been generally accepted as an entity in the last twenty years. Since then attention has been directed to its pathogenesis. The current trend is to regard the epidermal lesion as a secondary condition due to spread from an underlying carcinoma. Most of the cases recently reported had an underlying carcinoma, while in many of the earlier cases the lesion has been described as being localized to the epidermis. Weiner (1937), Huber, Gardiner and Michael (1951), Paget, Rowley and Woodcock (1954), Plachta and Speer (1954) and Rosser and Hamlin (1957), have each reported one case in which underlying carcinoma was present in the corium. These cases, together with the observation by Paget, Rowley and Woodcock (1954) and Lennox and Pearse (1954) that the Paget cells secreted mucin and therefore were probably not of epithelial origin, have led all the above authors to postulate that the lesion arises in an underlying carcinoma, and that the epidermal lesion is the result of upward spread from a carcinoma in the corium. The underlying carcinoma is stated by Lennox and Pearse (1954) and Rosser and Hamlin (1957) to arise in sweat glands while Paget, Rowley and Woodcock (1954) suggest origin in apocrine ducts and Weiner (1937), Huber, Gardiner and Michael (1951), Plachta and Speer (1954) and Eisenberg and Theuerkauf (1955) in apocrine glands.

The present paper describes two cases of Paget's disease of the vulva, one with the lesion limited to the epidermis and the other with underlying carcinoma in the corium. It is presented because study of our two cases suggests that the primary lesion arose in the epidermis and not in the corium. Paget's disease of the vulva is rare. According to Woodruff (1955), only 23 cases have been reported. Four cases (Dubreuilh, 1901; Rosenberg, 1909; Weiner, 1937; Huber, Gardiner and Michael, 1951) of these 23 were associated with underlying carcinoma. Since Woodruff the following have reported one case each without underlying carcinoma: Federici (1955), Lennox and Pearse (1954) and Haines (1955); with underlying carcinoma: Paget, Rowley and Woodcock (1954), Plachta and Speer (1954), Eisenberg and Theuerkauf (1955) and Rosser and Hamlin (1957).

CASE HISTORIES

Case 1

Mrs. M.K., a widow, aged 77 years, was admitted on 6th October, 1955. It was difficult to obtain a coherent history from her. She had had 10 children, of whom 7 were still alive. The menopause had occurred 27 years ago and there had not been any bleeding since. She had not suffered any previous illness. She complained of vulval irritation and discharge of at least 3-years duration. It had become more troublesome during the month before admission.

The patient was a stout woman, in good general condition, but with some impairment of her mental faculties. She had hypertension and some cardiac enlargement. The abdomen was obese.

The vulva (Fig. 1) was involved in a rash which was pale red in parts and brownish-red in others, it was moist, and in parts scaling,

particularly towards the periphery. The margin was sharply defined and polycyclical, slightly raised, extending to both genito-crural folds, the inferior part of the mons, the perianal region, and the adjacent part of the buttocks. All these areas were involved in one single lesion (i.e., there were no discrete patches). The affected skin appeared to be generally slightly swollen. There were no ulcers and no definite nodules. There was no enlargement of the inguinal lymph nodes.

Extended local vulvectomy was carried out with diathermy, with conservation of the anal sphincter. The incision was kept 2 to 3 cm. outside the involved area.

The patient's post-operative progress was satisfactory. The large wound was allowed to granulate and healed very well except for the anal region. She was discharged on 17th December. Follow-up has not shown any recurrence so far.

Pathology

Fifteen blocks were taken from the abnormal area in the vulva. The rest of the specimen was then cut up in slices of about 0·2 cm. in thickness, revealing no localized tumour. On microscopy all blocks revealed infiltration of the epidermis with Paget cells (Fig. 2), large rounded cells with abundant eosinophilic cytoplasm, sometimes vacuolated, and vesicular nuclei with large nucleoli. The cells were often found in a row, usually one or several cells thick, immediately above the basal layer. In some areas the row of cells was thicker, extending nearly throughout the whole thickness of the epidermis, where the cells were sometimes arranged in acini (Fig. 3). Occasionally the rows of cells had replaced the basal layer. The row of cells extended down into the rete pegs (Fig. 2) and hair follicles. Many of the cells contained mucin. Most of the rete pegs were lengthened and broadened and the epidermis in places showed hyperkeratosis and acanthosis.

Islands of carcinoma in the corium were found in eight of the fifteen blocks; they were not localized to any one area but were distributed fairly evenly throughout the specimen. Where found, islands were numerous and consisted of about six to sixty cells in the plane of a section. The cells in the islands were similar to the Paget cells in the epidermis and sometimes arranged in acini. The islands appeared just below the epidermis, probably invading from the epidermis (Fig. 4) or deeper down, possibly in lymphatics (Fig. 5). The corium contained many dilated small blood vessels, lymphatics and clusters of chronic inflammatory cells, mainly lymphocytes. No apocrine sweat glands were seen. The many eccrine sweat glands present were normal, but in some cases their ducts (Fig. 6) were dilated. In a few areas the ducts (Fig. 7) appear to be filled with carcinoma. In a few areas just below the epidermis, acini composed of pale eosinophilic cells (Fig. 8) resembling apocrine glands are present. These are thought to be metaplastic eccrine sweat ducts, because if followed in serial section they merge into normal eccrine sweat ducts; this type of change has also been suggested by Lennox (1954).

Case 2

The patient was a woman of 65 years who complained of pruritus vulvae of 8-years duration. It had recently become worse and had been treated with cortisone. She was seen by a dermatologist who diagnosed leukoplakia. She was referred for surgery in August, 1956. On examination at that time the appearances were those of extensive leukoplakic changes in the vulva. Simple vulvectomy was carried out. The patient was last seen in November, 1956. The area had healed but there was a small reddened patch outside the limit of excision on the left side.

Pathology

The epidermis was infiltrated by Paget cells (Fig. 9), some containing mucin as in Case 1. Four blocks were originally taken from this specimen and in none of these was an underlying carcinoma present. The rest of the specimen was blocked, cut at 6 μ and every tenth section examined, 643 slides in all; none of them contained any underlying carcinoma.

Discussion

Two cases of Paget's disease of the vulva have been described. One showed widespread underlying carcinoma; in the second case a very careful search failed to reveal any such carcinoma.

The origin of Paget cells in the epidermis of the vulva has long been controversial, but the modern trend is to ascribe them to spread from an underlying carcinoma of apocrine origin. Thus Rosser and Hamlin (1957) believe that they are metastatic in origin. In their case the carcinoma was in a small circumscribed area whereas the involved epidermal area was much larger. There was no evidence of spread via the lymphatics in the corium.

We feel that the absence of a carcinoma in the corium in our second case is against the current theory of an underlying tumour. The advocates of the origin from an underlying carcinoma believe that in cases of Paget's disease of the vulva where such a tumour was not found, a more thorough search might have revealed a small carcinoma. However the careful search in our second case answers this possible criticism and suggests that Paget's disease of the vulva can exist as a lesion which is localized to the epidermis. Furthermore, the long history of many of the cases is more suggestive of an intra-epidermal origin than of spread from an underlying carcinoma. The general layout of our first tumour also suggests origin in or near the basal cell layer and the closeness of much of the tumour in the corium, a spread from the epidermis downwards. It is, however, always difficult to be certain which way a tumour is growing. In our first case there is no convincing evidence that the tumour has arisen from eccrine or apocrine glands. As tumour can be seen in the ducts of eccrine sweat glands, there is a possibility that the neoplasm arose in these ducts, but we think the tumour invaded the ducts from the epidermis.

At first sight the view of Lennox, Pearse and Symmers (1952) that cutaneous tumours containing mucin arise, not from the epidermis but from sweat glands, seems to argue against an epidermal origin for Paget's disease. But when it is remembered that it is in the region of the basal layer that the primary epithelial germ arises which, according to Lever (1949), produces the apocrine sweat glands, it is possible that the cells of this region in the adult may still have the potentiality to produce a mucin-secreting tumour whose cells resemble those of apocrine glands. Further support for this theory is accorded by the observation of Lennox and Pearse (1954) that occasionally basal cell carcinomas secrete mucin.

We therefore suggest that the Paget's cells in the epidermis of the vulva arise *in situ* and the underlying carcinoma in our case is due to spread down from the epidermis. It may be that all the reported cases of Paget's disease of the vulva with underlying carcinoma are due to a downward spread from the epidermis, but it is not possible to exclude entirely a concomitant carcinoma arising from apocrine glands at some stage in the disease. For many of the cases of underlying carcinoma in the literature appear somewhat different from our case in that they are localized rather than generalized.

Summary

Two cases of Paget's disease of the vulva are described, one with and the other without underlying carcinoma in the corium. An underlying carcinoma in the second case was excluded by serial sectioning and examination of every tenth section.

The absence of underlying carcinoma in the second case suggests that the Paget cells arise *in situ* in the epidermis and not by spread from an underlying carcinoma which is the common theory at present. Furthermore the distribution of the underlying carcinoma in our first case suggests a spread downwards from the epidermis and not an origin in the corium.

We therefore suggest that vulval Paget cells originate in the epidermis. The underlying carcinoma in our first case probably arose by a spread downwards from the epidermis, but this may not always be the mode of origin of an underlying carcinoma which could also arise concomitantly from apocrine glands.

Acknowledgments

We wish to thank Dr. A. M. Barrett for his help in the preparation of this paper, Mr. O. Lloyd and Mr. W. R. Winterton for permission to reproduce the clinical histories, Dr. A. C. Thackeray for making available for examination the operation specimen of Case 2 and Mr. S. Patman for the photomicrographs.

FIG. 1

Case 1, Paget's disease of the vulva showing the extensive spread of the lesion, its polycyclical outline and variable appearance. (By permission of the Board of Governors of the United Cambridge Hospitals.)

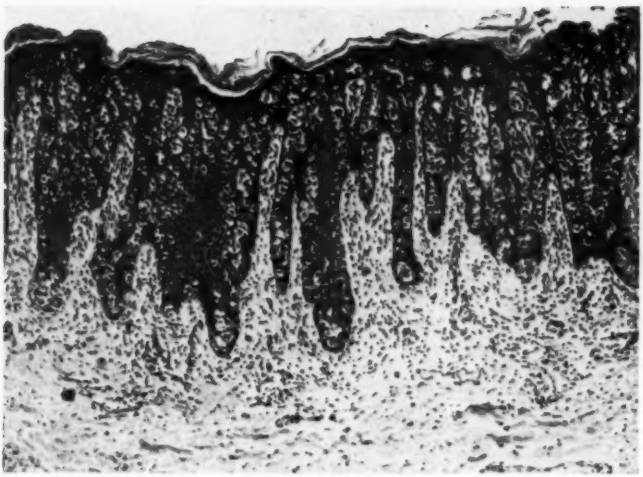

FIG. 2
Case 1, Paget's cells in epidermis. H. & E. ×75.

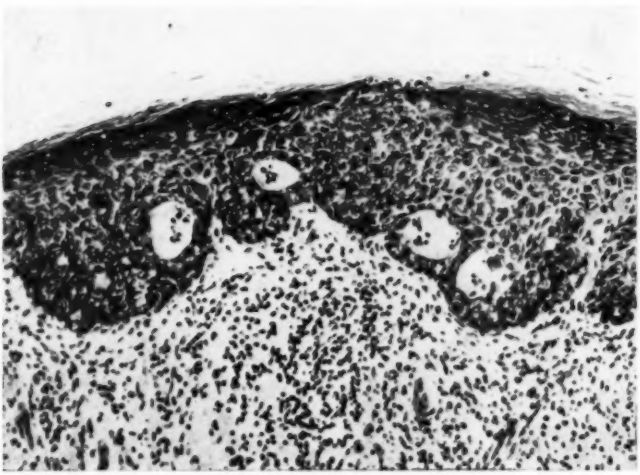

FIG. 3
Case 1, Paget's cells in epidermis showing acinar formation. H. & E. ×124.

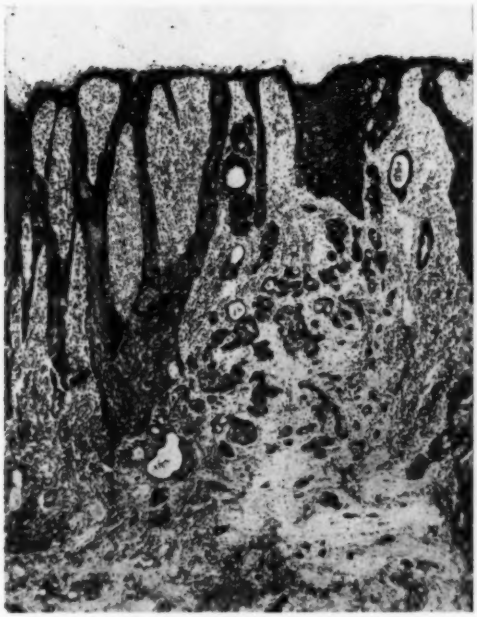

FIG. 4

Case 1. Islands of carcinoma in the corium, apparently spreading down from epidermis. H. & E. ×86.

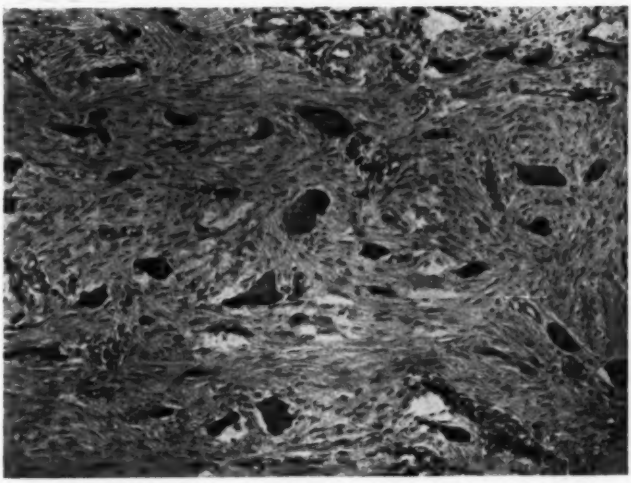

FIG. 5

Case 1. Islands of carcinoma cells in the corium. H. & E. ×124.

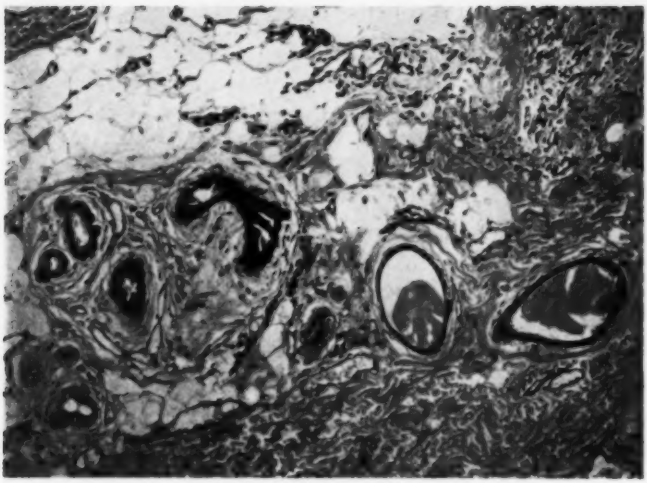

FIG. 6

Case 1. Dilated and normal eccrine sweat gland ducts. H. & E. ×154.

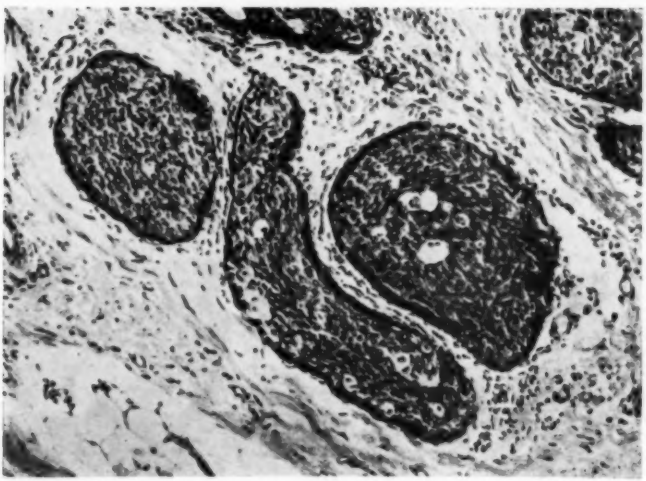

FIG. 7

Case 1. Dilated eccrine sweat gland ducts filled with carcinoma. H. & E. ×110.

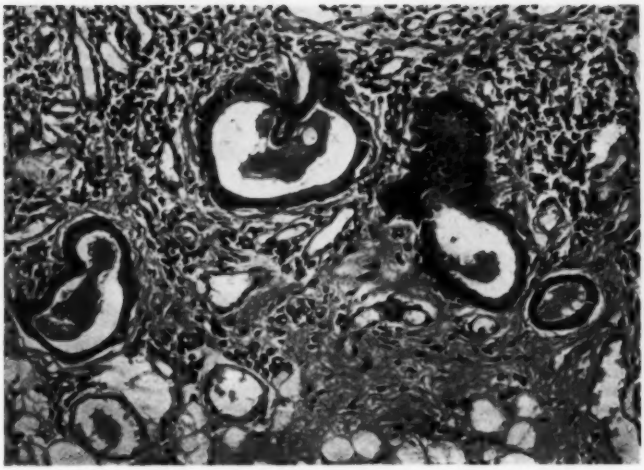

FIG. 8

Case 1. Metaplastic eccrine sweat gland ducts in which the cells resemble those of apocrine glands. H. & E. ×154.

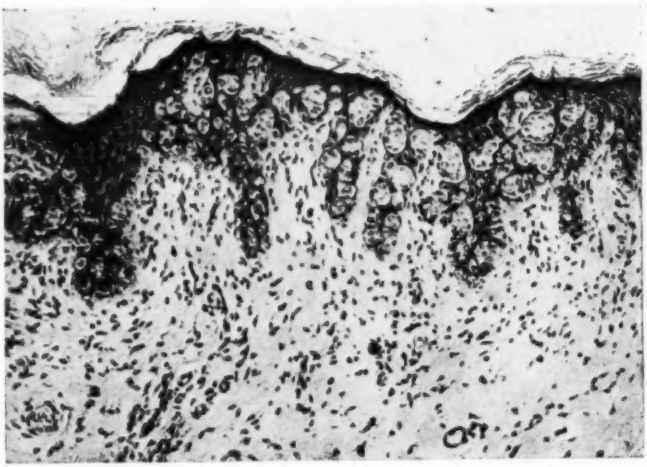

FIG. 9

Case 2. Paget cells in epidermis. H. & E. ×120.

We are greatly indebted to the Medical Committee of Addenbrooke's Hospital for contributing to the cost of the reproduction of the colour plate.

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BIOLOGICAL SEX DIFFERENCES WITH SPECIAL REFERENCE TO DISEASE, RESISTANCE AND LONGEVITY

BY

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NOT infrequently comment is heard regarding biological sex differences in the human and their relation to disease, resistance, longevity. This communication presents certain features of the two sexes in the ascertainment of their overall comparative biological status.

CHROMOSOMES

The male or female chromosomal content is transmitted by the fertilized ovum to every somatic cell. For over 30 years the number of chromosomes has been taken as 48 for every cell in the human body (Painter, 1924); however, recently it has been shown in cultures of foetal lung tissue, in spermatocytes and spermatogonia, and in adult tissues from the knee joint that the correct number of chromosomes is 46 (Tjio and Levan, 1956; Ford and Hamerton, 1956) (Fig. 1). The human female has two X chromosomes, the male an X and a Y. The Y chromosome is considerably smaller than the X (Painter, 1923, 1925; Evans and Swezy, 1929; Minouchi and Ohta, 1934; Hsu, 1952). Quantitatively, then, the male possesses less chromatin material in every cell than does the female, and presumably fewer genes.

There is a structural difference between human female and male somatic nuclei (Moore, Graham and Barr, 1953; Decourt *et al.*, 1954; Emery and McMillan, 1954; Hunter and Lennox, 1954; Hunter, Lennox and Pearson, 1954; Marberger and Nelson, 1954; Marberger, Boccabella and Nelson, 1955; Moore and Barr, 1954; Moore and Barr, 1955a). The difference between these nuclei is believed to depend upon the fusion of heterochromatic portions of the two X chromosomes of the female intermitotic cells to form one mass of chromatin. The X and Y chromosomes of the male somatic cell are apparently unable to fuse (Moore *et al.*, 1953). The mass observed in female somatic nuclei possesses characteristics which set it apart from the more generalized particles of chromatin. It is usually planoconvex in outline and is characteristically seen just within and in contact with the nuclear membrane (Moore, Graham and Barr, 1953). The average size of 100 sex chromatin bodies was found to be 0·7 by 1·2 microns (Moore and Barr, 1955b) (Fig. 2). A mass of comparable size, shape and position is not seen in human male somatic cells (Fig. 3).

SEX RATIO

It has been well established that throughout the world the sex ratio at birth is between 105 and 106 males to 100 females (Guttmacher, 1957). The cause for this universal differential in numbers of males and females has not been ascertained. It may well result from a difference in chromosomal content of the spermatozoa.

In a study of 5,787 embryos and foetuses corresponding to the third and seventh months of pregnancy it was found that the sex ratio was 108 males to 100 females (Tietze, 1948). A conception sex ratio of as high as 120 to 130 males per 100 females has been given (Boyd, 1947).

SEX HORMONES

The amounts of adrenal, ovarian and testicular hormones produced per day may be noted in

FIG. 1

Photograph of 46 intact human chromosomes in somatic cell. (Courtesy of Drs. J. H. Tjio and A. Levan.)

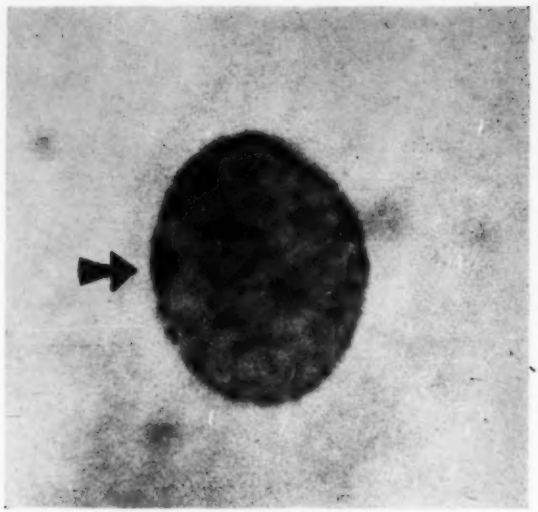

FIG. 2

Sex chromatin body of intermitotic nucleus in somatic cell from human female stained with a modified Feulgen technique.

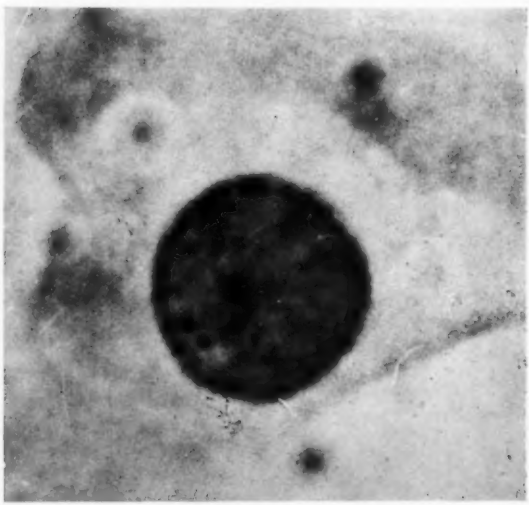

FIG. 3

Intermitotic nucleus in somatic cell from human male stained with a modified Feulgen technique.

Table I. The values for the female are representative for the third week of the menstrual cycle. Near the end of pregnancy oestrogens and progesterone are synthesized at the rate of approximately 50 mg. and 200 mg. per day, respectively (Vande Wiele).

TABLE I

Synthesis of Sex Hormones Per Day

Hormone	Female	Male
Corticosteroids ..	30–50 mg.	30–50 mg.
Testosterone	Trivial	3–6 mg.
Oestrogens	0·5–1 mg.	Trivial
Progesterone	30–50 mg.	Trivial

OTHER ENDOCRINES

The left adrenal gland is reported to be larger than the right (Schaeffer, 1953). During the first few years after puberty it is stated that the weight of the adrenal glands in the average weight female is greater than it is in the average weight male (Piersol, 1930). The adrenal cortex undergoes hypertrophy and contains an increased amount of lipoid substance during pregnancy (Beck, 1942).

The thyroid gland is cited as being larger in the female. There is an increase in size at puberty, during menstruation and pregnancy (Piersol, 1930).

Hypertrophy of the parathyroid glands occurs. Of 97 cases, 69 were females and 28 males. The increased incidence in females may result from hyperplasia of the parathyroid glands during pregnancy (Albright and Reifenstein, 1948).

The anterior lobe of the pituitary gland is larger in the female than in the male throughout life (Schaeffer, 1953). During pregnancy the pituitary gland may increase in size to twice normal, with hypertrophy primarily in the anterior lobe (Beck, 1942; Eastman, 1956). There is an increase in size of the gland with successive pregnancies, and after each gestation involution may not be complete, i.e., there may result a cumulative increase in size.

CONSTITUTION

In addition to the histological structure of those organs which make for sexual dimorphism, it is well known that the sexes differ in the specific weight, viscosity, packed cell volume and sedimentation rate of whole blood, as well as red blood cell count and serum iron content (Sandoz, Ltd., 1952). The cause for these differences has been a matter of some dispute. Several authors propose that menstrual blood loss is sufficient to explain them. Others maintain that the sexual differences in the blood may be hormonal in nature (Vahlquist, 1950). In the female coincidental with the menstrual cycle changes in body-weight occur, sometimes to the extent of 6 to 8 per cent, due primarily to general hydration.

The average weight of the male brain has been given as 1,360 g. or 48 ounces and that of the female as 1,250 g. or 44 ounces. Even though the weight of the brain in each of 15 outstanding men of the past is greater than the average for the male, there is no direct correlation between brain size and intelligence (Piersol, 1930).

After puberty the total quantity of fat is approximately 1·75 times as great in average weight females as in average weight males (Edwards, 1951). Women and men differ significantly regarding absolute fat and muscle content, fat distribution, and percentage of fat in relation to age. The amount of fat in the female body varies directly with increase in her age, whereas changes in men are normally insignificant with an increase in age. In general, fat and life-span are considered to bear an inverse relationship. There is the paradoxical situation in women, however, in that even with her opulent fat reserve at all age levels, her life expectancy continues to be greater (Garn and Saalberg, 1953).

Sex differentiation is evident not only in the topography and anatomy of the genito-urinary organs, but also in the dimensions of the head, trunk and appendages based upon anthropometric findings in important body measurements and indices (Wolff and Steggerda, 1943). Standing and sitting height, carrying angle of the elbow, outline of thoracic cage, width of shoulders, size and shape of neck, inclination and configuration of bony pelvis, weight of mandible, cranium and skeleton, shape of extremities, muscular development, hair distribution, cross section of hair, size of larynx,

length of intestines, weight of stomach, and centre of gravity differ for women and men (Schaeffer, 1953; McElroy; Keen, 1950).

The average weight of the heart in men is 312 g., in women, 255 g.; however, the heart is 0·53 per cent of body-weight in women and 0·43 per cent in men, that is, women possess on the average normally comparatively larger hearts (Piersol, 1930).

The basal metabolism of the female is about 3 to 5 per cent less than that of the male of the same age. The lower caloric output for females obtains for all ages (Werner, 1955).

The response of the body to change in temperature differs in women and men. Within the temperature range between 28° and 31° C. the nude male body can easily maintain the balance between heat loss and heat production. There is neither sweating nor shivering, and a male feels comfortable. This range of temperature, the comfort zone, is broader (27° to 33° C.) for women. In men under basal conditions the metabolism remains constant within the range of air temperature from 35° to 22° C. This is not true for women. Reduced heat production of from 14 to 20 per cent occurs in women between 30° and 32° C. Also, with the greater insulation afforded by the thicker layer of subcutaneous fat, the heat loss of the female body in a cold environment is 10 per cent less than that of men. Thus, women have a more efficient thermo-regulating mechanism than men, being better able, contrary to general belief, to resist cold and also to be more comfortable at higher temperatures with less perspiration (Best and Taylor, 1950).

Women, with a somewhat lower basal metabolic rate than men, expend less energy in muscular work. Accordingly, their food requirement is proportionately less (Best and Taylor, 1950).

After age 16, the distributions in strength for the two sexes overlap so little that practically no females reach the average performance level of males, and nearly all males are superior to the average of females. However, when woman's lung volume and vital capacity are taken into account, her ability to perform a maximum, muscular work is equal to that of man (Jones, 1947; Perman, 1953).

In normal individuals, the sense of hearing is superior in women until age 65, after which it is equal in the two sexes (Fowler).

The flow of tears in females from 16 to 29 years old is greater than in males. Beyond the age of 60, the reverse obtains (Henderson and Prough, 1950).

Observations on 274 healthy persons revealed that the serum cholinesterase of males is significantly higher than that of females (Reinhold, Tourigny and Yonan, 1953).

Plasma vitamin A and average carotene levels of normal men are higher than those of women ages 16–75 years. The statistical differences between the average plasma vitamin A levels of males and females indicate a sex difference in the physiologic dynamics which act upon the vitamin A. The sex difference in the average vitamin A level is believed to be one feature of the relations existing between vitamin A and the gonadal hormones. The age difference in the average vitamin A level, more marked in the female than in the male, is apparently related to the degree of gonadal activity (Hoffmann, Schneider and Quamo, 1950).

The electroretinogram in men and women in an ophthalmologically normal material consisting of 79 male and 52 female eyes in the age group 19 to 50 years showed a larger ERG for the female, 0·39 mV, than the male, 0·34 mV, a statistically valid difference, for which no explanation is known (Vainio-Mattila, 1951).

A linear discriminant function applied to fronto-occipital electroencephalograph recordings of left and right hemispheres of 50 normal females and 50 normal males, revealed a significant difference between females and males, more marked than between left and right hemispheres (Smith, 1954).

The sex incidence of congenital pyloric stenosis in 587 individuals per thousand live births of the same sex was 4·73 males and 1·12 females. There was no evidence of increased incidence of all other types of malformations in the affected children, or of association between pyloric stenosis and any particular malformation (MacMahon, Record and McKeown, 1951). In another study of 55 patients with congenital pyloric stenosis, the

sex ratio varied from 3 to 4 male children to 1 female child (Jones, 1956).

Reaction to Disease

Of 365 pathological conditions, 245 occurred more often in males and 120 more often in females. Endocrine and skin disturbances were predominant in women, in contrast to gastro-intestinal, vascular, lymphoid, skeletal, nerve, muscular, urinary, respiratory, metabolic and infectious diseases in men (Hamilton, 1948). Mortality is higher in males of all ages from pneumonia, bronchitis, appendicitis, peptic ulcer, coronary heart disease (Johnstone and Hosker, 1948).

In Sweden, Germany, England, France and the U.S.A. tuberculosis has a statistically more serious prognosis for men. After 25 years of age there is a decrease in the incidence of the disease, affecting women more favourably than men. A further rise occurs among men, and between ages 40 to 60 considerably greater mortality obtains among them. Prognosis is far better following thoracoplasty in women than in men (Dahlberg, 1944).

Taking pregnant patients into consideration, in the adult group poliomyelitis is preponderant in the female (Weinstein, Aycock and Feemster, 1951). Also, figures of reported cases of the disease show the incidence of paralysis higher in females (Benjamin and Taylor, 1951). However, the duration of urinary retention associated with acute poliomyelitis is longer in male than female patients (Weatherby and Steigman, 1953).

Between the ages of 40 and 70 years diabetes mellitus is significantly more common in women than in men, the ratio being approximately 3 to 2. In earlier life there is a slight preponderance in males (Cecil and Loeb, 1955). Cholelithiasis, toxic and non-toxic goitre are more prevalent in the female. Women with more frequent hypertension have a longer lifetime.

The distribution of new cases of cancer by sex and primary site in New York State shows that, except for genital and thyroid cases, the incidence is greater for the male in the buccal cavity, digestive, respiratory, urinary, lymphatic and central nervous systems, brain and skin (N.Y. State Dept. Health, 1954). Nearly all diagnoses are confirmed in New York State by microscopic examination. Consequently the incidence of cancer based on diagnoses reported in New York State is very nearly true.

In 650 major abdominal operations the course of the anaesthesia was completely satisfactory in 65 per cent of the women and 48 per cent of the men. Respiratory and circulatory post-operative complications were, on the whole, twice as common in men as in women. Respiration in women is predominantly costal in type. Accordingly, an abdominal wound reduces respiratory exchange less in the female than in the male. Consequently she is less likely to develop a post-operative pulmonary complication. Hiccough occurs more in men during anaesthesia and post-operatively than in women. Paralytic ileus is far more common in men than in women (Gordh, 1950; Perman, 1953).

A study of the deaths associated with anaesthesia and surgery based on 599,548 anaesthesias in 10 institutions in this country between 1948–1952 inclusive revealed that of the 384 deaths 58 per cent occurred in males and 42 per cent in females (Beecher and Todd, 1954). In general, women have been cited as better operative risks (Papper, 1957).

In 1954, as in preceding decades of this century, white females had the better record for longevity in this country. Their expectation of life at birth rose to 73·6 years, compared with 67·4 years for white males; for the non-white population, the corresponding figures were 65·8 and 61·0 years, respectively (Metropolitan Life Insurance Co., 1956).

Since 1900 the gains in expectation of life have been largest in childhood and least at older ages. The average remaining lifetime at age 20 increased about 8 years for males and 12 years for females. At age 45, the corresponding gains were 3·3 and 6·7 years. In 1955, the life expectancy at age 65 was 13·1 years for white males and 15·7 years for white females (Metropolitan Life Insurance Co., 1956).

Comment

The greater resistance of the female sex is exemplified by her longer life. The shorter life span of males is characteristic throughout the animal world. In 42 species, including invertebrates, vertebrates and mammals, the females

outlive the males (Hamilton, 1948). This should be kept in mind when differences in modes of life and habits would be cited as factors resulting in the difference in longevity in man and woman.

It has been concluded that the same type of curve encountered everywhere for the increased death rate of men in the higher age groups is indicative of an inferior power of resistance, instead of special conditions regarding the population (Dahlberg, 1944).

The possibility that woman's reliable supply of gamma globulin, the blood fraction that contains the antibodies against infectious diseases, is related to the fact that women live longer than men has been considered. The lack of gamma globulin in the blood is not uncommon in men but is very rare in women (Zbar, Cippes and Alterman, 1956).

Endocrine and glandular changes in the female normally are perfectly synchronized with her meeting stress in one of her most important roles in life, bearing offspring. To ensure conception, in the male there is a far greater biological wastage in germ cells. The male governs what the offspring will be, male or female, but it is done at his expense.

Mortality occurs *in utero* in 20 to 30 per cent more males than females (Boyd, 1947). Also, during the first years of life more males succumb than females (Gordh, 1950). Accordingly, the explanation for the overall higher male mortality is not to be found, e.g., in exertion, the often dangerous work of men, the abuse of alcohol and tobacco.

With respect to somatotype, or bodily form, marked quantitative differences exist between the two sexes (Sheldon, Stevens and Tucker, 1940; Sheldon, Dupertuis and McDermott, 1954). Women are more endomorphic than men, heavier in proportion to stature at all ages, and yet of lower specific gravity. For a sample of 4,000 young women of 18, the mean index of height over the cube root of weight was 12·85. For a parallel sample of 4,000 young men of 18, this index was 13·19. The mean somatotype for this series of women was 5–3–3½, where the first digit refers to endomorphy, the second to mesomorphy, and the third to ectomorphy. For the men the mean somatotype in this series was 3½–4–3½. Since the standard deviations for these primary components (endomorphy–mesomorphy–ectomorphy) range from about 0·8 to about 1·2 in both sexes, it would appear that in endomorphy women surpass men by more than a standard deviation, while men are more strongly endowed with mesomorphy to an equal degree. The two sexes are at the same level in ectomorphy. This work on somatotyping raises the interesting question whether the known superior viability of women may be related to their lower degree of mesomorphy. In the later expression of their somatotypes women, with their greater endomorphy, diverge even farther from men with respect to the height-weight ratio (Sheldon *et al.*, 1940, 1954). The mere putting on of fat in itself, then, may not be as deleterious an event as we have sometimes supposed it to be. Perhaps the danger lies, rather, in putting on of fat in the face of high endowment with mesomorphy.

Why more males than females are conceived is not known. The Y chromosome is smaller than the X. Consequently the Y-containing spermatozoon is lighter and may well have a smaller head. The smaller head could permit more rapid migration to and penetration of the ovum. With the difference in size of the sex chromosomes, the total gene content is not the same in the two sexes. This difference in total number of genes most likely is reflected in the different biological aspects of males and females. Possibly the female with XX chromosomes carries factors for longevity not present in XY chromosomes of the male.

Observations on animal and human castrates show that testicular secretions contribute to the lesser viability of males, increase their metabolism and exert widespread effects throughout the body (Hamilton, 1948). When exposed to whole body X-irradiation, intact male mice with the normal quota of testosterone have less survival value than do castrated males. Castrated males injected with the female hormone, oestradiol benzoate, exhibit maximum survival (Rugh and Wolff, 1956) (Fig. 4).

Male mice are more radiosensitive than are females of the same strain, regardless of the phase of the oestrous cycle in which the females are X-irradiated. The females in oestrous are most radio-resistant; those in dioestrous are

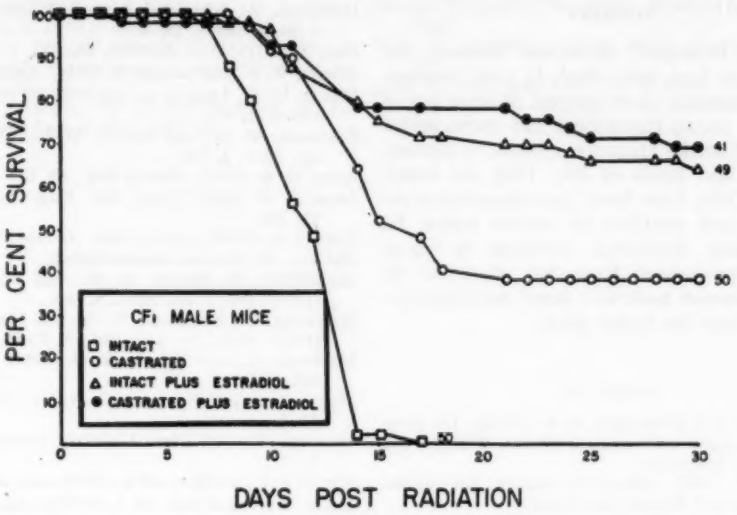

FIG. 4

Sensitivity of male mice to X-irradiation. Animals exposed to 625 r whole body X-irradiation in numbers and categories noted. Oestradiol benzoate, 0·166 mg. in 1·0 ml. of sesame oil, injected intraperitoneally. (Courtesy of Dr. Roberts Rugh.)

most radiosensitive (Fig. 5). Hypersecretion of oestrogens during oestrus and the correlated endocrine and hydration changes at this time may afford the increased resistance (Rugh and Wolff, 1956). The exact manner in which oestrogens exert the protective action against radiation is not known. Also, why testosterone is inefficient in protecting against radiation and is deleterious in the intact radiated animal is not understood (Treadwell, Gardner and Lawrence, 1943; Patt *et al.*, 1949; Graham and Graham, 1950; Ellinger, 1954; Rugh and Clugston, 1956).

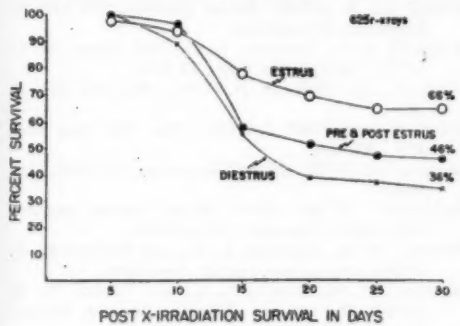

FIG. 5

Radiosensitivity with respect to the oestrous cycle in the mouse. Survival curves after an exposure of 625 r in 150, 2–3 month-old female mice. (Courtesy of Dr. Roberts Rugh.)

Oestrogen administration increases phospholipids and the alpha/beta lipoprotein ratio; it decreases cholesterol and the cholesterol/phospholipid ratio, all of which are believed to be factors in atherogenesis. Coronary atherosclerosis is from 10 to 40 times as frequent in men under 40 as in women under that age, in whom coronary disease hardly ever occurs. Oestrogens given to males favourably alter the lipoprotein spectrum, even in individuals after myocardial infarction (Griffith, 1956).

The potassium content of the body is higher in males than females, related to the fat content which contains no potassium. Consequently, the per cent of the potassium which is radioactive is greater in the human male, in whom a greater deleterious effect is possibly exerted (Spiers *et al.*, 1956).

Summary

Various biological differences between the human sexes have been cited. In every population fewer females are conceived. *In utero* and in every age group throughout life more males succumb. Females are more resistant to disease, the stress and strain of life. They are better operative risks, have fewer post-operative complications and continue to outlive males. In general their biological existence is more efficient, pre-eminent than that of males. In brief, the human male with beard and functioning testes pays the higher price.

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THE REPAIR OF RECTO-VAGINAL INJURIES

BY

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RECTO-VAGINAL injuries are less often seen than formerly, due to the rising standard of obstetric care, but they are still by no means uncommon. In spite of advances in anatomical and physiological knowledge together with therapeutic advances, there has been little change in the approach to the problems of repair of these injuries for many years.

ANATOMY

Milligan and Morgan described the anatomy of the anal canal and the lower end of the rectum in detail and with great clarity (Milligan and Morgan, 1934, 1937; Milligan, 1942) and the relevant points in their description are summarized in Figure 1.

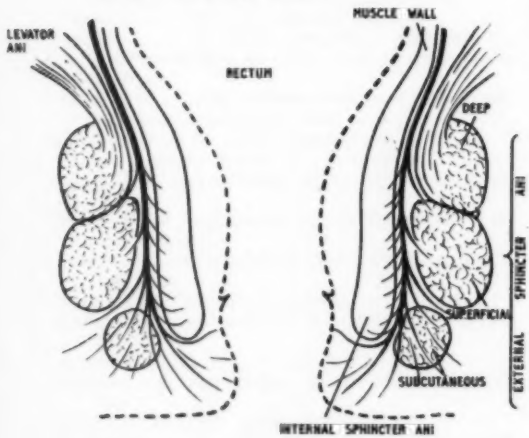

FIG. 1

Shows the arrangement of the sphincter muscles at the anus.

More recently Goligher, Leacock and Brossy (1955) have modified this description with conclusions which are of great interest in such procedures as haemorrhoidectomy and the treatment of anal fissure, but are not of such great significance in the present problem. These authorities contest Milligan's view that the external sphincter shows a division into subcutaneous, superficial and deep parts (see Fig. 1), We believe that the findings in obstetric injuries and at operative dissection of the female perineum consistently show these divisions quite clearly.

It will be noted that the external sphincter ani forms a cuff of voluntary muscle surrounding the anal canal and ano-rectal junction, while the internal sphincter is the thickened lower end of the circular muscle coat of the rectum, i.e., involuntary muscle.

PHYSIOLOGY

The rectum is normally empty and is filled intermittently by mass peristalsis of the colon which forces gas and faeces around the angle of the pelvi-rectal junction. The distension of the rectum gives rise to a feeling of fullness and a desire to defaecate, but, unless the distension is very forcible and rapid this desire has not any element of urgency. If control is asserted voluntarily by the contraction of the external sphincter and the levatores ani, the initial desire for defaecation passes off, the accumulation of further faecal material, giving the rectum a reservoir action a little similar to the urinary bladder. The study of the sensibility of the rectum and colon by Goligher and Hughes (1951) showing its vital importance in the maintenance

of anal continence is of great help in the understanding of this mechanism. We would extend the ideas expressed by these authors. As faeces accumulate in the rectum they press to a lower level until they impinge on the epithelium lining the anal canal; here a different type of sensation is appreciated producing, in the patient who is not habitually constipated, an urgent desire to pass a motion. Once again this may be inhibited but with considerably more effort, by the will acting through the external anal sphincter; if the motion is loose this control may not be completely effective even then.

A further activity of the external anal sphincter is that of emptying the anal canal intermittently during defaecation, and finally at the end of a motion.

In the light of this account of the anatomical and physiological factors, it is possible to analyze the types of anal incontinence produced by injuries to the anatomical structures concerned.

Anal Incontinence and Recto-Vaginal Injuries

(1) The obstetrical injury known as a third degree perineal tear often involves the subcutaneous part (the "umbrella ring") of the external sphincter alone. Cases are frequently seen in the gynaecological clinic where repair of the subcutaneous sphincter has not been successful, leaving a "horse-shoe" appearance of this divided sphincter. In these cases continence is unimpaired because the repair of the perineal body anterior to it has healed successfully.

(2) A second degree of severity is the laceration which extends to the perineal body, the subcutaneous and superficial parts of the external sphincter and the ano-rectal wall. Failure of repair here usually leads to incontinence of flatus and failure to control loose motions.

(3) The most severe tears extend through all of the external sphincter including the deep part, which fuses with the levatores ani. All voluntary control of the motion must now be lost, but the result to the patient depends on other factors also. Owing to the intermittent filling of the rectum, incontinence here cannot be compared as a disability to the constant loss of urine in bladder fistulae. Provided the rectal sensibility remains unimpaired, prompt action by the patient at the first feeling of distension, provided that the motion is solid, usually leads to the avoidance of gross soiling. Of additional assistance are good bowel habits which may be developed so that mass colon evacuation occurs regularly at certain times of the day.

There may well be a type of case where the tear of the rectal wall is so extensive that the stimulus of distension is interfered with and complete incontinence results from failure to receive any warning of the arrival of the faeces.

Two other symptoms common in severe recto-vaginal injuries are urgency and frequency of defaecation. Urgency may be understood as the necessity to resort to the lavatory at the first sign of rectal distension so as to avoid soiling. The frequency may well be the result of this early emptying of the rectum leading to the loss of its "reservoir" function.

There would appear to be another source for these symptoms in the condition called by Greenhill (1955) "diastasis of the levator ani pillars", which may occur in the absence of any externally obvious laceration of the anal sphincter. In these cases it may be that the loss of supportive action of the levatores with the deep part of the external anal sphincter, leads to the rapid descent of the faeces from the upper rectum so that they impinge on the anal canal and produce the urgent call to stool previously described.

Treatment

It is now proposed to reconsider methods of treatment:

(a) *Recent Recto-vaginal Tears*

The most striking feature of severe lacerations at delivery is the extraordinary power of healing of the puerperal perineum as a result of hormone induced vascularity and the strong local immunity to autogeneous infection. Failure is, therefore, due to faulty technique or to the introduction of exogeneous infection. The orthodox methods of repair produce excellent results, but the traditional type of after-care with the bowels confined for from 5 to 10 days, followed by an agonizing ordeal with the first

hard motion, is open to criticism. At this time the catgut sutures are more or less digested and weakened, and tissue adhesion is still far from strong.

If liquid paraffin is given from 12 hours after repair, with a saline aperient after 24 hours, a loose easy motion is achieved while all sutures are at their strongest; regular easy bowel movements are maintained from then on. Eastman (1950) lends indirect support to this when he states "Despite older ideas to the contrary, third degree lacerations require no special attention in the puerperium except that enemas should be withheld".

(b) *Old Standing Recto-vaginal Lacerations*

These are a much more difficult problem because atrophy and contracture of the tissues has occurred, particularly if the menopause has supervened; healing is also poor because the scarring reduces vascularity and the hormone effects of pregnancy are lacking. Success is best obtained by applying the knowledge of the anatomy and physiology now available, by remembering the excellent behaviour of the tissues in the puerperal cases, and by the proper application of general surgical principles. If this is done there should be no need to carry out a preliminary colostomy.

Case Reports

Four cases are briefly reported to bring out the application of these principles.

Case 1. Mrs. O.M.B., aged 58 years, para-5

This patient sustained a severe obstetric injury to the perineum 34 years before admission; since then there had been complete faecal incontinence mitigated only by constipation. An attempt to repair the tear one year after its infliction had failed. A characteristic disability was that, if the constipation became severe requiring a purgative, the patient "darè not leave the house until her bowels had been opened", as she had no control when the sudden colon peristalsis filled the rectum.

Before operation the perineum was absent with the tear running through the lower third of the vagina into the anal canal and rectum for an estimated three inches above the original anal opening.

Pre-operative preparation with oestrogen (Ethinyl oestradiol 0·01 mg. b.d.) was begun two days beforehand, and combined with a penicillin-streptomycin preparation (Crystamycin), this treatment being maintained post-operatively also.

At operation the subcutaneous part of the external sphincter was atrophic and shortened to about half an

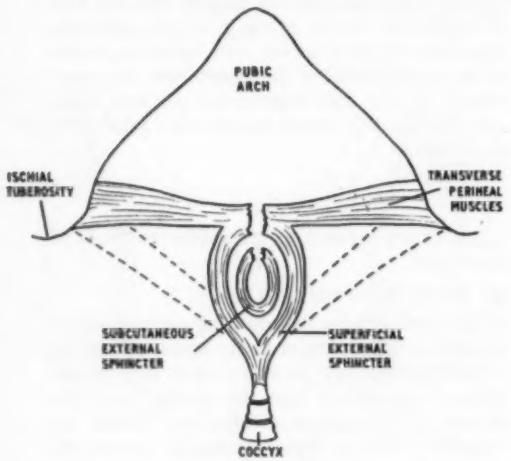

Fig. 2

Shows the immediate effect of a mid-line tear on the superficial and subcutaneous parts of the external anal sphincter. Owing to the fusion of the transverse perineal muscles with the superficial part of the central point of the perineum, retraction in old lesions is as shown by the dotted lines.

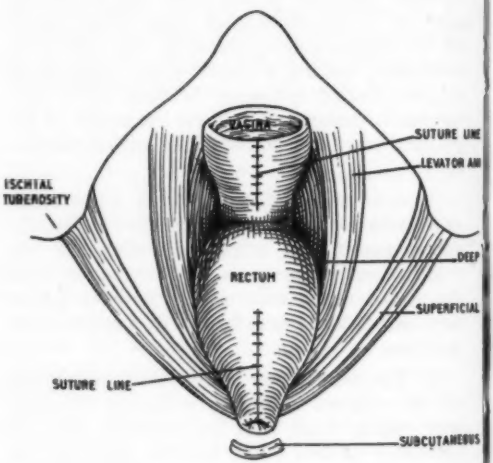

Fig. 3

Shows muscular sphincters exposed during the repair o chronic tear: the vagina and anal canal have been mobilized repaired.

inch; the shortening was such as to make it quite impossible to stretch it to encircle the anus. Deeper dissection revealed the superficial part of the external sphincter extending from the sides of the anal canal outwards to the ischial tuberosities. Consideration of the anatomy of the transverse perineal muscles will explain how trauma dividing them in the midline, followed by retraction, leads to this state of affairs (Fig. 2). By detachment of this muscle from the ischial tuberosities a muscle strip is produced which will easily encircle the anal canal (Fig. 3). The vaginal walls were then freely mobilized and reconstituted followed by similar treatment of the rectum and anal canal; the importance of free mobilization and union without tension cannot be over-emphasized. Next, deep catgut sutures were inserted to draw the levatores ani muscles together particularly at the posterior ends where the deep part of the external anal sphincter is thus reformed. After further mobilization the skin edges were approximated with as little tension as possible.

Post-operatively the oestrogens were continued for 14 days and penicillin-streptomycin for 10 days; on the second night liquid paraffin was given followed by a saline aperient next morning. Convalescence was complicated by a deep femoral thrombosis, but the repair healed soundly with complete continence. Digital dilatation of the rectum was repeated intermittently for 3 months to overcome the tendency to contracture owing to the rigid post-menopausal tissues, and the result was then entirely satisfactory.

Case 2. Mrs. M.R., aged 42 years, para-1

This patient complained of urgency and frequency of defaecation since a forceps delivery 12 years ago. The bowels were opened three or four times a day but the patient was usually able to avoid soiling herself if she could get to the lavatory "within a minute or two". There was no control of flatus and there was a constant mucoid discharge from the anal region causing soreness. An attempt had been made to repair the trouble one year after the delivery, but this had broken down. It was characteristic that the patient had come to accept her disability as incurable and had so adjusted herself to living with it that her trouble was only discovered when she was seen with another, and more trivial complaint.

There was a complete tear of the perineum with rectal mucosa forming the posterior margin of the vaginal introitus; the tear of the anal canal extended about two inches above the anal margin. The repair of the recto-vaginal tear was performed on the same lines as described in the previous case except that the penicillin-streptomycin was omitted. Healing was satisfactory apart from the development of a stitch abscess just anterior to the anus, which cleared up after the discharge of a little pus. On discharge after three weeks, the operative result was very satisfactory; the frequency of defaecation was reduced to a daily motion, and control of flatus was satisfactory. The patient was asked to delay emptying the bowel for half an hour after the desire to defaecate was felt and she reported that she was able to manage this quite easily.

Case 3. Mrs. M.B., aged 26 years, para-2

This patient sustained a complete recto-vaginal tear 3 years before as the result of a forceps delivery; a poor repair left her with a recto-vaginal fistula. She was seen when she booked for her second pregnancy when she was found to have a fistula which admitted the tip of the index finger about 2 inches above the anal orifice; the subcutaneous part of the external anal sphincter showed the typical horseshoe appearance due to failure of union. She was allowed to proceed with a vaginal delivery and, when the head descended on the perineum, a finger was passed per rectum into the fistula and the perineum was incised in the midline on to this finger, thus reproducing the original complete tear. After delivery of the baby and placenta, scar tissue was excised and repair carried out under local anaesthesia, in the usual manner. The subcutaneous sphincter presented a very different picture to that of the post-menopausal patient of Case 1; it was still a substantial and elastic structure, which could be readily drawn round the reformed anal canal and repaired with a modified mattress suture. This suture is of some importance; after an ordinary mattress suture has been formed the end is passed through the loop of the mattress (Fig. 4). The result is a stitch which

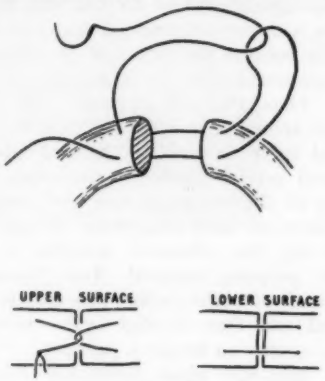

FIG. 4

Modified mattress suture for repair of subcutaneous sphincter.

unites the divided ends without any tendency to eversion or inversion, thus giving an effective union.

Twelve hours after delivery liquid paraffin was given followed by a saline aperient 24 hours later; the patient was kept in bed for 10 days to avoid the shearing stresses of ambulation. Healing was by first intention, and the functional result has been completely satisfactory.

Case 4. Aged 41 years, gravida-5

Tear occurred at first delivery 21 years ago, and there were 3 further deliveries over the next 10 years. Six months prior to her being seen in the out-patient department, she had had a further delivery, this being 10 years

after the birth of the previous child. Her confinement was normal in every way and she sustained only a superficial skin laceration of the perineum. Examination revealed a complete recto-vaginal tear of old standing, obviously dating back to the earlier pregnancies; despite this, the patient gave a clear history of freedom from symptoms until after the recent delivery. Since then she had lost control of flatus and loose motions, with urgency of defaecation even with the normal motion. A repair operation relieved these troubles successfully and the photograph (Fig. 5), which demonstrates the superficial part of the external anal sphincter, was taken with this patient.

The case demonstrates how well with regular bowel habit a patient can manage with only the deep part of the sphincter intact. It is assumed that the last delivery, when the tissues had lost much of the elasticity of youth, led to a diastasis of the levatores ani and the attached deep anal sphincter, without any gross external laceration.

Discussion

Clinical observations and results of treatment in recto-vaginal injuries do not tally in many respects with current textbook accounts. This is basically because the nature of anal continence and incontinence has not been generally understood. Thus the subcutaneous part of the external sphincter is often referred to as "the external sphincter ani", and inordinate stress is placed on its repair. In fact, loss of the activity of this muscular ring has remarkably little effect on anal continence, though this is not to say that, whenever possible, it should not be properly repaired. The "paradoxical operation" of Miller, where this muscle is first repaired and then divided again—with good results—seems no longer a paradox!

The relatively good functional results of operations, where the anatomical results have not been satisfactory, has been puzzling in the past. This becomes understandable when one appreciates the essentially intermittent quality of faecal incontinence, and the preponderating importance of the deeper part of the repair. These factors also explain the surprising tolerance developed by patients with severe recto-vaginal lacerations.

Summary

The account in current gynaecological textbooks of the symptomatology and treatment of recto-vaginal injuries takes insufficient account of more recent knowledge of the anatomy and physiology of this region. There is undue stress on the subcutaneous part of the external anal sphincter, and the traditional post-operative routine is open to criticism.

Recent obstetric recto-vaginal injuries repaired by accepted techniques heal well owing to the hormone-induced vascularity of pregnancy. It is often the best time to repair pre-existing chronic tears and fistulae. Early opening of the bowels should be encouraged.

In old-standing complete tears and fistulae oestrogens can be used to reproduce the favourable effects of pregnancy. In chronic and post-menopausal cases it is impossible to reconstitute the subcutaneous external sphincter, but this is of little importance. The deeper superficial part can be identified and used in lieu with special care in the repair of the deep external sphincter ani and the pubo-rectalis portion of the levatores ani.

Post-operative care should be directed to early and easy bowel action as in recent tears.

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FIG. 5

Note scissors behind the superficial part of the external anal sphincter which runs from the ischial tuberosity behind the anus. The finger is placed in the anal canal.

A CASE OF FATAL ANTE-PARTUM PULMONARY EMBOLISM WITH POST-MORTEM EXTRACTION OF A LIVE BABY

BY

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POST-MORTEM Caesarean section is the oldest known major surgical operation.

In the year 715 B.C. the Roman Senate decreed that no woman advanced in pregnancy was placed in the sepulchre until the child had been removed from her body by this operation. This was done by the Romans so that baby and mother might be buried separately. During the Christian Era it was performed so that the baby might receive the blessing of baptism.

There are no reports concerning successful results of this procedure until the last century. During the 19th century Pfaff (1916) states that of 331 post-mortem Caesarean sections performed only 6 or 7 live babies were delivered.

During the first fifty years of the 20th century there has been greater success; so far there are approximately 80 cases of post-mortem Caesarean sections with extraction of a live baby.

The cause of death in the majority of cases was some complication of pregnancy, notably toxaemia and convulsions. Other fatal causes include cerebral haemorrhage, pneumonia, cardiac failure, dissecting aneurysm, bulbar poliomyelitis and tuberculosis.

CASE REPORT

A multipara, aged 33 years, presented at the Antenatal Clinic early last year. Her three previous children were delivered vaginally without complications.

Clinical examination revealed no abnormality and her uterus corresponded in size to the period of amenorrhoea.

Subsequently she attended the Antenatal Clinic and apart from excess weight gain which responded to diet she progressed satisfactorily.

During the last trimester, when the uterus was that of a 38-weeks pregnancy, she complained of pain and tenderness in her right thigh. On examination she had a thrombophlebitis of her right saphenous vein. She was admitted to hospital for bed rest and the local application of heat. The pain and tenderness subsided after two days. At this stage her abdominal findings were vertex presenting, head not fixed, longitudinal lie, fundus at term. The foetal heart was normal and foetal movements easily felt. Her blood pressure was 130/90 mm. of mercury, and her urine clear.

At 6.55 p.m. the next day she was found in the toilet by a nurse apparently having "a fit". She was taken to the labour ward and when seen she was deeply cyanosed and frothing at the mouth. No respiratory movements were discernible and resuscitative methods were applied without success. It was apparent that the most likely cause of the collapse would be a pulmonary embolus.

Death was confirmed on further examination and a post-mortem Caesarean section was performed.

A lower midline incision was made followed by a classical incision into the uterus. The uterus was firm and tightly applied to the baby.

The baby, weighing 8½ pounds, was of reasonably fresh colour with a heart rate of 120. Respirations were slow to commence but after 5 minutes regular breathing began. Apart from some irritability for twelve hours the baby progressed satisfactorily and was discharged from hospital 2 weeks later. He smiled at 3 months and crawled at 8 months. At 9 months (1st May, 1957) he weighed 25 pounds 8 ounces,

pulled himself up into the standing position and is very bright and intelligent.

The post-mortem findings of the mother revealed deep congestion of both lungs. Within the pulmonary artery an embolus was found which commenced one centimetre above the pulmonary valve, and extended into the right and left branches as far as the next division.

In the inferior vena cava three centimetres below the liver a small thrombus four centimetres in length was lying free within the vein. The right saphenous vein was distended by adherent thrombus. The pelvic veins, femoral veins and left saphenous vein were patent.

Discussion

Pulmonary embolism in pregnancy is a rare occurrence. No cases have previously been reported where post-mortem extraction of a live baby has been performed in a case of fatal pulmonary embolism.

In maternal mortality reports from the United States clinics quoted by Collins and Nelson (1946) the incidence of fatal pulmonary embolism varied between 4·7 and 20 per cent of all obstetric deaths. All of these deaths occurred either intra-partum or post-partum.

Dieckmann (1942) states that, of the circulatory changes in the pregnant woman, some tend to increase and others to decrease the liability to venous thrombosis. For example, while there is an increase in the blood fibrinogen and fibrin by as much as one-third, there is a decrease in the platelet count. Following delivery there is an increase in the platelet count as after operation.

Experiments by Wright, Osborn and Edmonds (1950) showed there was an increased venous pressure in the legs in pregnancy and a slowing of the circulation. It is known that varicose veins in pregnancy may be associated with a superficial thrombophlebitis.

Maternal pulmonary embolism due to amniotic fluid has been widely reported. At autopsy often no significant gross abnormality is found. Microscopically the diagnosis is established by the demonstration of extensive vascular occlusion by leucocytes and constituents of amniotic fluid in the smaller branches of the pulmonary arteries.

In these cases the membranes have always been ruptured allowing escape of the amniotic fluid into the uterine cavity before symptoms of embolism occur.

Sections of the lungs in some of these cases showed the degree of embolism to be small and not extensive enough from a mechanical point of view to explain death. An anaphylactic reaction has been advanced as the cause of death but as yet no definite proof has been forthcoming from experiments or animal studies.

In contemplating extraction of the baby post-mortem, consideration must be given to the time interval following the death of the mother.

In this case the time interval between the death of the mother and extraction of the baby was 8 minutes, and it is doubtful if the baby could have been resuscitated if there had been much more delay.

It is reported that a live baby can be extracted up to 25 minutes after maternal death. This interval is probably too long for most cases, even where the mother was previously healthy.

Another factor to be considered is the cause of the death of the mother. The foetal prognosis is considered better where maternal death is rapid than where there has been a long continued illness, and also when the period of gestation is near term.

Summary

(1) A case of fatal ante-partum pulmonary embolism with the extraction of a living child is reported for the first time.

(2) Ante-partum pulmonary embolism is rare, although it is not so uncommon post-partum.

(3) The embolus arose from a superficial saphenous vein thrombosis, the symptoms being pain and tenderness over the vein.

(4) A reasonable time interval exists for extraction of the baby following the death of the mother.

(5) Three factors affect the chances of survival of the baby:

(*a*) The time interval between death and extraction of the baby.

(*b*) The period of gestation.
(*c*) The cause of maternal death.

ACKNOWLEDGMENTS

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THE SIGNIFICANCE OF SOME UNUSUAL FOETAL CARDIAC ARRHYTHMIAS

BY

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IT is accepted without question that irregularity of the foetal heart is a sign of foetal distress, when that irregularity is produced by rapid variations in the rate.

This paper, however, is concerned with far less common aberrations. It is based upon nine cases in which premature beats, dropped beats and persistent regular bradycardia were heard from the foetal heart during labour.

Extra-systoles are not considered to be of great significance in the young person, although they may appear or increase in frequency due to stress, lack of sleep, etc.: they are not usually associated with cardiovascular lesions. Heart block may be associated with a defect in the interventricular septum or occur as a temporary derangement in the course of, or in convalescence from, an acute illness (Beaumont, 1945).

With these facts in mind, anyone hearing these irregularities from the foetal heart during labour might wonder whether they indicate foetal distress or the presence of congenital heart disease.

CASE HISTORIES OF PRESENT SERIES

A. *Cases with Both Evidence of and Cause for Foetal Distress*

(1) *M.D.* (1948). For ten minutes there were frequent irregular premature beats with an overall rate of 80 per minute before delivery: there was also thick meconium. Caesarean section was performed for prolapsed cord. After delivery auricular extra-systoles were confirmed by E.C.G.—about 3 per minute. Two months later there was no evidence of congenital heart disease, but occasional extra-systoles were still heard.

(2) *E.N.* (1948). Early in labour there was complete cardiac irregularity associated with thick meconium. Delivery was by Caesarean section, and a short cord round the baby's neck was a possible cause for the foetal distress. Frequent auricular premature beats were heard after delivery and confirmed by E.C.G. at 4 weeks old. The baby was followed up until one year old, when the rhythm was normal, and no evidence of congenital heart disease appeared.

(3) *F.W.* (1948). There were occasional premature beats throughout a 13-hour labour, which was terminated by low forceps under pudendal block when the foetal heart rate rose to 174 per minute: a tight true knot in the cord was found. Premature beats were still heard immediately after delivery but no E.C.G. was done: they had gone at 4 days old. There was no evidence of congenital heart disease when examined at one month.

(4) *E.B.* (1956). Surgical induction of labour for hypertension was performed at 38-weeks gestation. Premature beats varying in frequency between 1 in 2 and 1 in 6 were heard: the foetal heart rate began to rise to 150 per minute, and eventually Caesarean section was performed when no labour had occurred, 48 hours after artificial rupture of the membranes. No premature beats were heard after delivery, and the baby appeared normal.

(5) *N.N.* (1957). A regular bradycardia had been heard from the 35th week of pregnancy, throughout labour at full term and until the baby died when 4 days old: the rate varied between 48 and 80 per minute. The liquor was meconium-stained during labour. An E.C.G.

after delivery demonstrated complete dissociation between auricular action (136/min.) and ventricular (48/min.). Post-mortem examination revealed an interventricular septal defect.

B. *Case with Cause for but no Evidence of Foetal Distress*

(6) *J.D.* (1955). During the last 10 hours of a prolonged labour at 42-weeks gestation, premature beats were heard at a frequency varying between 1 in 5 and 1 in 30. The baby was born alive by Caesarean section, and premature beats were still heard after delivery: they had ceased by the time the baby was 4 days old.

C. *Cases with Neither Evidence of Nor Cause for Foetal Distress*

(7) *M.C.* (1948). Two abnormal rhythms were heard at different times towards the end of labour; these were the dropping of every fourth beat and a pulsus bigeminus. After a normal delivery extra-systoles were heard, till at least 9 days old, and were shown by E.C.G. to be from a nodal or auricular ectopic focus. Examination at 10 months old gave no evidence of congenital heart disease.

(8) *A.S.* (1948). Premature beats were heard at a frequency of 1 in 3 before a normal delivery, and they continued immediately after delivery. At 3-months old there was a normal rhythm and no evidence of congenital heart disease.

(9) *G.S.* (1948). A regular bradycardia varying in rate between 60 and 112/minute occurred throughout labour. After a normal delivery auricular extra-systoles, 1 beat in 3, were confirmed by E.C.G.: they were still present at 4 months. Examination when 4-years old revealed no evidence of congenital heart disease or abnormal rhythm.

Analysis of the Case Records

(1) *What Significance can be Attached to the Presence of Premature Beats?*

Out of the 8 cases with premature beats before or shortly after delivery, 4 had definite evidence of, and cause for, foetal distress, and one more had cause for such distress but without other evidence. Only 3 cases had neither. No case had evidence of congenital heart disease.

(2) *The Persistence of Extra-systoles after Delivery*

(a) *Six cases had premature beats before delivery:* in 5 of these the condition persisted after delivery for varying periods before finally disappearing.

	Premature Beats	
When Last Heard	*When No Longer Heard*	
2 months later (infrequent)	No further record	(M.D.)
Immediately after delivery	4 days later	(F.W.)
Immediately after delivery	14 days later	(J.D.)
9 days later (infrequent)	10 months later	(M.C.)
Immediately after delivery	3 months later	(A.S.)

(b) *Two cases had premature beats after delivery but not before: these persisted as follows:*

	Premature Beats	
A.N. Finding	*Last Heard*	*Not Heard*
Complete irregularity	4 weeks later	9 months later (E.N.)
Slow regular rhythm	4 months later	4 years later (G.S.)

Thus, whether premature beats are an indication of foetal distress or not, they may persist after delivery for some time, 4 months being the longest in this series.

(3) Three cases showed possible *evidence of heart block in utero*

(M.C.) with every fourth beat dropped.

(N.N.) and (G.S.) with a regular bradycardia.

In two of these, (M.C.) and (G.S.), no evidence of heart block or congenital heart disease was found after delivery. Extra-systoles, however, were heard up to 9 days and 4 months respectively. No other evidence of, or cause for, foetal distress was apparent.

In the third case (N.N.), the slow regular rhythm persisted after delivery until the baby died when 4 days old. E.C.G. demonstrated a complete heart block and post-mortem examination proved the presence of an interventricular defect. (This is the only case in which extra-systoles were never heard.)

Literature

(1) *Foetal Extra-Systoles*

Hyman (1930) made a phonographic study of the foetal heart and picked up 6 cases of dropped beats due to extra-systoles. The actual ectopic beat was not audible to the ordinary stethoscope, but an E.C.G. after delivery confirmed the diagnosis. The irregularity soon disappeared, the longest time being 8 days. He concluded that the condition had no special clinical significance, and that its discovery by the obstetrician should cause him no undue concern.

There have been a few records of antenatal extra-systolic arrhythmia which, however, ceased at birth, the child being apparently normal (Cohn, 1906; Hecht, 1913; von Reuss, 1914; Seitz, 1916; Riehl, 2 cases, 1926; Holtermann, 1928; Schroeder, 1929).

On the other hand, Dippel (1934), described 2 cases of foetal extra-systoles in which the children, when born, were cyanosed and soon died; post-mortem examination showing multiple cardiac irregularities. The first case exhibited a recognizable systolic murmur which enabled the diagnosis of a heart lesion to be suspected before delivery. The second case presented as a regular bradycardia antenatally, with a rate of 50 per minute. After delivery, an E.C.G. showed a pulsus bigeminus, each normal beat being followed by an extra-systole: the clinical bradycardia was still present as the extra systole was ineffective.

Roberts (1938) also described a case with foetal extra-systoles and a recognizable systolic murmur, which died 42 hours after delivery with a congenital heart lesion.

(2) *Partial Heart Block in the Foetus*

Maclellan (1935) described a case with a dropped beat after every 4 to 8 normal beats. The baby was cyanosed after delivery and died after 6 months; autopsy showed only a patent foramen ovale, no record being given on the histology of the Bundle of His. The case was diagnosed as one of heart block by Dr. MacKenzie (Professor of Medicine) and Dr. Murray (Cardiologist), although no specific mention of an E.C.G. is made.

Kriszt (1937) reported a case of partial heart block in the foetus of 2:1 or 3:2 variety before delivery and 4:3 or 3:2 afterwards, confirmed by E.C.G. The irregularity was still present on the 10th day, but had gone by the time the baby was 4 months old. The child appeared to be quite healthy.

(3) *Complete Heart Block in the Foetus*

This has been reported 13 times (including one case in the present series), where the diagnosis has been confirmed by E.C.G. after delivery. These cases have been set out in Table I.

Other cases of regular bradycardia in pregnancy and labour have been recorded, but the opportunity for performing an E.C.G. was not provided. Sankey (1948) described such a case in which the bradycardia was heard immediately after delivery but had gone by the sixth day: this infant had a murmur, typical of Maladie de Roger, but appeared otherwise to be well. Case (G.S.) in the present series is another example, the bradycardia ceasing after delivery.

The confusion that can arise between heart block and foetal distress has been referred to (Geiger and Hines, 1940; Sankey, 1948; Riley, 1949; Harris, 1952).

With regard to prognosis, Riley (1949) states that "the presence of complete auriculo-ventricular block combined with other evidence of congenital heart disease has been associated with short duration of life in the cases so far reported".

(4) *Detection of Heart Murmurs in the Foetus*

Massman (1854) appears to have recorded the first case of a murmur detected in the foetus, confirming the heart lesion later at autopsy.

Hoehne (1903) reported a case of his own and studied 7 more from the literature. He suggested criteria for the diagnosis of a heart lesion *in*

TABLE I

Complete Heart Block Diagnosed Antenatally and Confirmed After Delivery by E.C.G.

Case No.	Author	How Long Before Delivery When First Heard	When Last Heard After Delivery	Comments
A. Cases with Good Prognosis (2 cases): (Healthy babies in which the block disappeared and there was no evidence of an organic heart lesion.)				
1	Heubner (1938)	No record	11 months	Alive and well.
2	Hammond, Stone and Hyams (1944)	1 month	No record	Alive and well.
B. Cases with a Reasonably Good Prognosis (4 cases): (Healthy babies in which the block persisted for as long as the child was observed, but in which there was no other evidence of an organic heart lesion.)				
3	Geiger and Hines (1940)	17 hours	5 months	Alive and well.
4	Ottow (1939)	24 hours	5 months	Alive and well.
5	Thomson (1943)	2½ months	4 years	Alive and well.
6	Harris (1952)	2 weeks	8 weeks	Alive and well.
C. Cases with Bad Prognosis (7 cases):				
7	Sankey (1948)	9 hours	7 weeks	Systolic murmur typical of I.V. septal defect. Died at 4 months.
8	Riley (1949)	11 days	6 months	Loud rasping systolic murmur. Heart much enlarged.
9	Thomson (1943)	7 hours	1 year (Died)	Healthy till death at 1 year. No septal defect at post-mortem.
10	Yater (1929)	2 weeks	10 days (Died)	Multiple congenital defects at post-mortem.
11	Plant and Steven (1945)	5 weeks	6 days (Died)	No Purkinje fibres at post-mortem.
12	Redman (1958)	5 weeks	4 days (Died)	I.V. septal defect at post-mortem.
13	Witt (1934)	2 months	75 days (Died)	Coarctation of the aorta at post-mortem.

All babies were born alive by the vaginal route.

utero: there should be a constant rough murmur localized over the point of maximum audibility of the foetal heart with an occasional failure of the heart sound.

Sampson, McCalla and Kerr (1926), Dippel (1934) and Roberts (1938) also found a foetal systolic murmur useful in predicting congenital heart disease.

DISCUSSION AND CONCLUSIONS

(1) *Premature Beats Heard from the Foetal Heart*

It would appear from the present series that extra-systoles are indicative of some degree of foetal distress, but not of congenital heart disease. The obstetrician would be well advised in these cases to have a very close watch kept for more definite signs of distress.

This optimistic view is supported by opinions from the literature, except that in 2 cases (Dippel, 1934; Roberts, 1938), the premature beats heralded a congenital heart lesion. In both cases, however, a systolic murmur gave an antenatal clue. This particular sign might be deliberately listened for in these cases to give help in prognosis, particularly when a decision involving the baby is to be made.

(2) *Dropped Beats Heard Antenatally*

These might be due to regular but ineffective extra-systoles, or to partial heart block. The case in the present series (M.C.) might have been either, for the arrhythmia was not heard after delivery. However, even proven partial heart block can disappear, as in Kriszt's case, leaving no evidence of a heart lesion. Perhaps it is a reaction to the stress of labour.

On the whole, there would seem good reason for being optimistic here, too, while being alert for foetal distress developing and listening for a foetal murmur.

(3) *Regular Foetal Bradycardia*

Undoubtedly this can be due to a true heart block, as in the 13 cases listed in the table: 6 of these babies had a reasonable prognosis and 7 a bad one. As disappearance of the block as late as 11 months has occurred (Heubner, 1938), it might still do so in at least three of those in whom it was persisting when last seen.

Another possible cause for the bradycardia might be regular, ineffective extra-systoles, alternating with a normal contraction, as in Dippel's second case (which died of a severe heart lesion). Case (G.S.) in the present series might have been another example, particularly as frequent extra-systoles were recorded after delivery (the baby here appeared to be normal).

The complete disappearance of a heart block is most surprising, especially after so long an interval as 11 months. No satisfying explanation can be offered for this phenomenon.

At any rate, whatever the cause for the bradycardia, an uneventful delivery of a living child can be anticipated: no child in this collected series was stillborn.

The obstetrician faced with the problem of regular foetal bradycardia must not confuse it with severe foetal distress, and usually no special action is called for. If, however, drastic action should be indicated on behalf of the baby, the chances of the child being grossly abnormal are about "evens". Not even the time for which the condition has been detected before delivery is of assistance, for in 3 out of the 6 "good prognosis" cases, the bradycardia had been noted for two weeks or more. Foetal electrocardiography is feasible, but the tracing is too intricate, because of the superimposed maternal record, to do much more than demonstrate the rate of the foetal heart (Smyth, 1957).

Summary

(1) A series of 9 cases showing foetal arrhythmia is presented.

(*a*) Six cases exhibited foetal extra-systoles. In one of these cases, on another occasion, a 4:3 dropped beat rhythm was heard.

(*b*) Two cases had a regular foetal bradycardia: in one of these extra-systoles were heard after delivery.

(*c*) In one case there was complete irregularity of the foetal pulse with extra-systoles postnatally.

(2) A study of the literature on the subjects of foetal extra-systoles, foetal heart block (partial and complete), and heart murmurs in the foetus, has been made.

(3) The conclusions reached as to the significance of these arrhythmias are as follows:

(*a*) The prognosis with foetal extra-systoles is reasonably good. Congenital heart disease is unlikely, but the condition may be regarded as showing some evidence of foetal distress calling for closer observation.

(*b*) A 4:3 dropped beat rhythm, also, need not be of serious significance.

(*c*) With regular bradycardia, about half the cases available for study had a poor prognosis, and about half had a reasonably good one. All were born alive. Even when complete heart block is demonstrated after delivery, it may still eventually disappear, leaving an apparently normal heart.

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A SAFE METHOD OF KIELLAND'S FORCEPS DELIVERY

BY

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THE correction of the persistent occipito-posterior and deep transverse arrest of the foetal head can be the most formidable manipulation in operative obstetrics and an unrecognized or uncorrected posterior position of the foetal head is still the most common cause of "failed forceps" (Feeney, 1947). In the average pelvis the midcavity provides the maximum available space for the head to rotate and this is normally assisted by the descent of the head on to the pelvic floor. This mechanism can be reproduced by the use of Kielland's obstetric forceps, which are always applied correctly to the foetal head and in which the descent of the head down the birth canal often progresses during rotation. The Kielland's obstetric forceps are a potentially dangerous instrument in the hands of those unfamiliar with the subtle variations of the birth canal and of the spatial relationship between the forceps blade and handle. When used correctly and with gentleness they can achieve an atraumatic, controlled delivery with an ease remarkable to those experienced in the difficulties of manual manipulation. A perfect application can always be achieved with the head stable and low in the pelvis. A mildly contracted pelvis does not provide sufficient space for the hand to lie alongside the foetal head in the pelvic cavity; the forceps blades are thinner and are more easily accommodated. The head can be moved upwards or downwards in the cavity of the pelvis until the level of easiest rotation is found.

Unlike manual rotation there is no possibility of pushing the head free above the pelvic brim with the inherent dangers of high forceps application. Rotation is performed slowly under complete control and without risk of the head slipping back to the occipito-posterior position. Only with Kielland's forceps can asynclitism be easily corrected.

GENERAL OBSERVATIONS ON TECHNIQUE

General anaesthesia sufficient to relax the muscles of the pelvic floor is essential. The patient is placed in the lithotomy position with the buttocks overhanging the delivery bed and this permits the shank of the forceps to be pressed against the tip of the coccyx during rotation. The bladder is emptied and the perineum stretched sufficiently to allow palpation of the foetal skull with four fingers. The operator sits (Longaker and Harriman, 1927) and the Kielland's forceps are assembled in front of the patient with the concavity of the pelvic curve and indicator knobs directed towards the foetal occiput. This represents the position of the forceps after their final application. In transverse positions of the foetal head the anterior blade is selected and applied first. Contrary to current teaching (Jones, 1952) an episiotomy is unnecessary for application of the forceps and the rotation of the head. Serious vaginal lacerations may result from extension of an episiotomy performed too early and the perineum should not be incised until the head is crowning and the handles have assumed a horizontal position.

THE RIGHT OCCIPITO-LATERAL POSITION

Application of the Anterior Blade

The handle is held 20 degrees above the horizontal and is pressed firmly against the posterior aspect of the thigh. Using two fingers as a guide the anterior blade is well lubricated with antiseptic cream and is inserted into the vagina directly over the sinciput until the angle of the fenestration disappears from sight (Fig. 1).

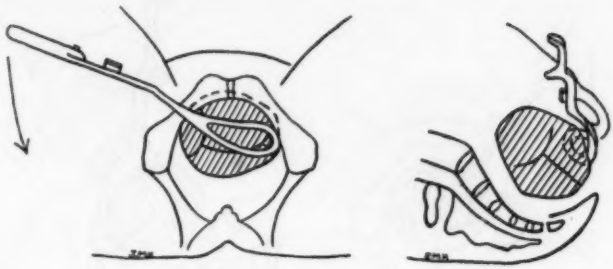

FIG. 1

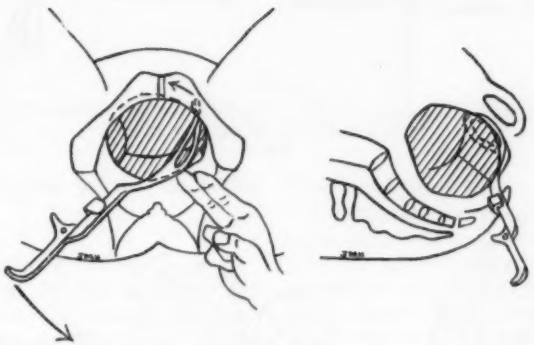

FIG. 2

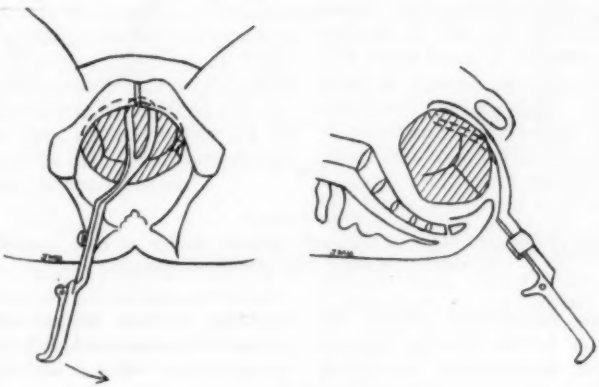

FIG. 3

FIGS. 1, 2 AND 3

Application of anterior blade of Kielland's obstetric forceps in right occipito-lateral position of the foetal head.

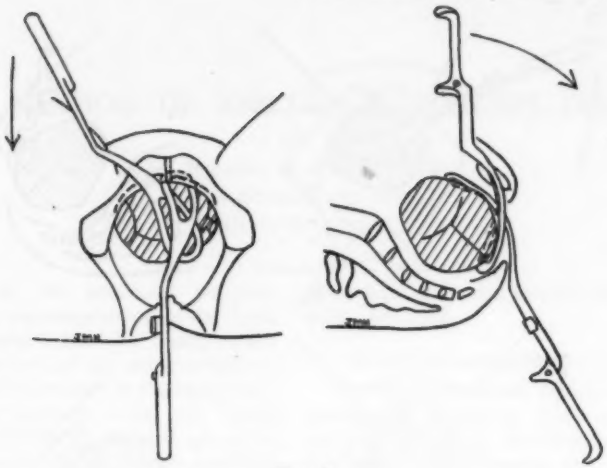

FIG. 4

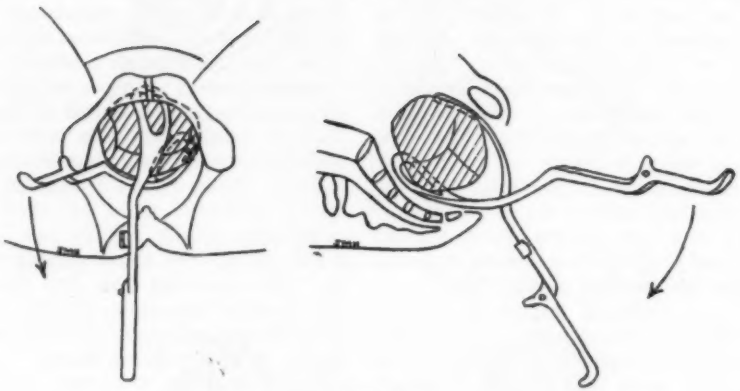

FIG. 5

FIGS. 4 AND 5

Application of posterior blade of Kielland's obstetric forceps in right occipito-lateral position of the foetal head. Continued opposite.

The blade is now manœuvred behind the symphysis pubis on to the anterior parietal bone. This is best accomplished by slowly swinging the forceps in an arc around a fulcrum formed by a finger pressed against the lower border of the blade at the angle of the fenestration (Fig. 2). The leading edge of the blade is directed slightly towards the scalp and away from the anterior vaginal wall. No resistance should be encountered and, if the space behind the symphysis pubis is limited, more room can be obtained by pushing the head slightly upwards. Failure to keep the handle pressed against the thigh while it is swung downwards is the usual cause of difficulty. When the anterior blade is in position the handle will make

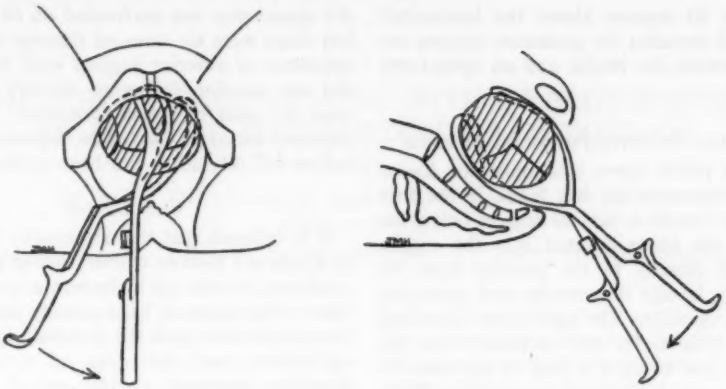

FIG. 6

Application of posterior blade of Kielland's obstetric forceps in right occipito-lateral position of the foetal head, continued.

an angle of 60 degrees to the horizontal (Fig. 3).

Application of the Posterior Blade

The handle is held 70 degrees above the horizontal and the posterior blade is introduced into the vagina beside the pelvic curve of the anterior blade (Fig. 4). Using two fingers as a guide the handle is swung slowly downwards and outwards towards the operator. The blade slides on to the posterior parietal bone and in front of the left sacro-iliac joint (Fig. 5). When the tip of the posterior blade is above the pelvic brim it is pushed gently to the midline (Fig. 6). If the blade were kept in the midline the tip would impinge against the sacral promontory and difficulty would be encountered.

Locking the Blades

The shanks are brought together taking care to exclude the perineum. Asynclitism is corrected by gentle digital traction on the posterior shoulder of the handle downwards at 60 degrees to the horizontal. The handle lock (Holmes, 1957) may now be inserted and this will permit a firm grip of the handle without any tendency to crush the head and will produce perfect alignment of the blades with no risk of slipping.

Rotation of the Head

The handles are kept depressed at 60 degrees to the horizontal and the head is pushed upwards ½ inch to relieve impaction (Cordua, 1931). The application of the forceps is checked and if found correct rotation is begun. Unless the handle lock is used the forceps must be gripped in front of the shoulders. The head is rotated very slowly between uterine contractions and ample opportunity is given for the vaginal mucosa to slide over the surface of the forceps and foetal head. If difficulty is encountered the head is pushed upwards towards the pelvic brim and rotation again attempted. The level of easy rotation always lies above the plane of arrest and radiological pelvimetry may provide valuable assistance in finding the optimum level. On rare occasions it may only be possible to rotate the head above the plane of the pelvic brim, but as a perfect cephalic application has already been acquired the dangers of high forceps need not be feared.

Traction

After the biparietal application has again been checked traction is made on the distal shoulders in the axis of the birth canal. This is at first downwards at 60 degrees below the horizontal and finally, as the head is crowned,

upwards at 20 degrees above the horizontal. As the head stretches the perineum scissors are inserted between the blades and an episiotomy performed.

The Direct Occipito-Posterior Position

With the pelvic curve and indicator knobs directed downwards the left blade is the first applied. The handle is held 20 degrees below the horizontal, the blade inserted into the vagina and applied directly to the parietal bone by swinging the handle downwards and outwards towards the operator. The right blade is applied in a similar fashion. On rare occasions when the head is only just engaged it may be necessary to wander the right blade over the sinciput. Even when the head is high the classical method (Kielland, 1916) is never indicated and is potentially dangerous.

Results

During the years 1952–57 Kielland's forceps delivery has been performed on 72 occasions and this represents an incidence of 18 per cent of forceps deliveries personally performed or supervised. Some were cases of failed forceps admitted as emergencies, many were cases where residents had attempted manual rotation without success. Apart from 2 macerated foetuses, 2 cases of foetal death during the first stage of labour and one gross abnormality incompatible with life, there were no foetal deaths. There were no failures and all infants were successfully delivered occiput-anterior. An episiotomy was performed on 66 occasions, but there were no cases of damage to the anal sphincter or anterior vaginal wall. Haematuria did not develop following delivery and there were no cases of fistula formation. The cervix required suture in two cases following delivery before full dilatation had been achieved.

Conclusion

It is believed that the notoriously bad results of Kielland's forceps delivery in the past can be attributed to their use in desperate circumstances when other methods have already failed and by those unfamiliar with the elaborate technique of application and the rules of rotation. The specialist practised in the art of Kielland's forceps delivery can effect a safe, atraumatic vaginal delivery in situations where other methods are associated with much foetal and maternal trauma and even total failure.

Acknowledgments

I wish to express my thanks to the Consultant Obstetric staffs of Guy's Hospital, Newcastle General Hospital and Farnborough Hospital on whose patients the deliveries were performed.

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THE USE OF ERGOMETRINE WITH HYALURONIDASE TO PREVENT POST-PARTUM HAEMORRHAGE

BY

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DESPITE many advances in obstetrics, post-partum haemorrhage continues to contribute to maternal mortality and morbidity. Over the years many different factors in the causation of post-partum haemorrhage have been pointed out, so that nowadays it is possible to recognize many patients who present a particular risk of third stage complications. It is possible to select such patients for individual attention in the third stage and, on the whole, the results achieved are satisfactory.

Nevertheless, there are still a large number of patients in whom post-partum bleeding arises as an unexpected event. In recent years, the routine administration of ergometrine with the birth of the baby has been frequently advocated as a prophylactic measure to reduce the numbers of such unexpected haemorrhages. The results obtained with ergometrine given by the intramuscular route have not been sufficiently striking to justify its routine use (Flew, 1947; Daley, 1951). Intravenous ergometrine has been shown to be more effective in reducing the incidence of post-partum haemorrhage (Lister, 1950; Martin and Dumoulin, 1953), but this method has the disadvantage that an assistant must be available to give the injection at the right moment. In 1954 Kimbell claimed that the addition of the enzyme hyaluronidase to ergometrine given intramuscularly accelerated the absorption of the oxytocic, and produced a prompt uterine response similar to that obtained following the intravenous injection of ergometrine. This author reported a large series of cases in which ergometrine (0·5 mg.) with hyaluronidase (1 mg.) was given intramuscularly with the birth of the anterior shoulder. The post-partum haemorrhage rate was reduced from 6·4 per cent to 0·9 per cent by this method. The present paper describes the results obtained with ergometrine and hyaluronidase at the City General Hospital, Sheffield.

PRESENT INVESTIGATION

An investigation was planned to determine the effect of the routine intramuscular injection of ergometrine (0·5 mg.) with hyaluronidase (1 mg.) given to a group of normal patients with the birth of the anterior shoulder. (The combination of drugs used was that produced by Evans Pharmaceuticals, Ltd., called "Ergo-rondase". This is a convenient term and is therefore used hereafter in this paper.) Two groups of patients were studied, a group of 500 cases receiving prophylactic Ergo-rondase were delivered in the University Unit at the City General Hospital and a control group of 707 cases were delivered in Dr. W. J. Clancy's Unit at the same hospital, this being a convenient initial method of selection.

Only normal cases in which third stage complications were not anticipated were included in the investigation. The following cases were therefore excluded: patients delivered under general anaesthesia, forceps deliveries, grande multiparae (gravida-six or more), cases of ante-partum haemorrhage, labours exceeding 48 hours in the first stage or two hours in the second stage, multiple pregnancies, cases of hydramnios, patients with a history of primary or secondary post-partum haemorrhage or of manual removal of the placenta, congenital malformations of the uterus, foetal death *in utero* or any other condition which could be associated with defective blood coagulation. Breech deliveries were excluded because of the

difficulties of timing the Ergo-rondase injection. Cases of extreme prematurity were not included. Anaemic patients (haemoglobin less than 10 g. per cent) were excluded because they usually received prophylactic intravenous ergometrine.

All the patients were delivered in the lithotomy position by midwives or by students or pupil-midwives under supervision. In the control group, the baby was delivered slowly between pains. The fundus was lightly guarded until signs of separation appeared and the placenta was expelled. Ergometrine (0·5 mg.) was given intramuscularly at the end of labour. If intrapartum bleeding of 10 ounces (284 ml.) or more occurred, the fundus was controlled and the doctor called. If the bleeding persisted and a doctor was not immediately available ergometrine (0·5 mg.) was given by intramuscular injection. If the placenta was still retained after 45 minutes, whether there was bleeding or not, a doctor was called and preparations made for manual removal.

In the Ergo-rondase group, a freshly prepared injection was kept on the delivery trolley. The unassisted midwife gave the injection after freeing the anterior shoulder between pains. When available, an assistant gave the injection.

After the baby had been completely delivered, provided the uterus was found to be contracting strongly and even if the classical signs of separation were not present, a gentle attempt was made to express the placenta. This was usually quite easy but, if not, the case was conducted as in the control group; the procedure for dealing with abnormal cases was also the same. Ergometrine was not given after the birth of the placenta unless haemorrhage occurred. If the Ergo-rondase was not given with the anterior shoulder, it was not given at all.

Results

The control and the Ergo-rondase groups were first re-examined for possible sources of bias which might reduce the value of any comparisons to be made. The groups were similar in age distribution. No medical attendant was found to be particularly associated with the abnormal third stages. The groups were not similar in parity distribution, the proportion of primigravidae in the control group (59·3 per cent) exceeding that in the Ergo-rondase group (55·6 per cent). This was because the bookings for Dr. Clancy's Unit were slightly greater, particularly for primigravidae.

In order to determine whether or not the difference in the parity distribution between the two groups would unduly influence subsequent comparisons, the post-partum haemorrhage rates in the control primigravidae and the control multigravidae were compared (Table I). The primiparae had a post-partum haemorrhage rate of 6·2 per cent compared with 2·1 per cent in the multigravidae, a difference which is statistically significant. This suggests that a normal primipara is more likely to get a post-partum haemorrhage than a normal gravida 2–5. Therefore, it was felt that any comparisons between the control and the Ergo-rondase groups should be made with the primigravidae separated from the multigravidae.

Table I

Incidence of Post-partum Haemorrhage in Normal Primigravidae Compared With Normal Multigravidae

	Post-partum Haemorrhage	No Post-partum Haemorrhage	Totals
Primigravidae	26 (19·9)	393 (400·1)	419
Gravidae 2–5	6 (13·1)	282 (274·9)	288
Totals ..	32	675	707

Chi-square = 6·7. P less than 0·01. (Expected numbers in brackets.)

Post-Partum Haemorrhage

In primigravidae, the incidence of primary post-partum haemorrhage (a measured loss of 20 ounces (568·2 ml.) or more) was 6·2 per cent in the controls and 2·5 per cent in the Ergo-rondase group, a difference which is statistically significant (Table II).

In the multigravidae, the post-partum haemorrhage rate was 2·1 per cent in the controls and 2·7 per cent in the Ergo-rondase group, a difference which is not statistically significant. There was also evidence that the severity of the post-partum haemorrhage in the Ergo-rondase cases was less than in the control cases. Thus, only 1 of the 13 Ergo-rondase cases lost more than 30 ounces of blood and no blood trans-

TABLE II
Primary Post-partum Haemorrhage in Primigravidae

	Post-partum Haemorrhage	Per cent	No Post-partum Haemorrhage	Totals
Controls ..	26 (19·8)	6·2	393 (399·2)	419
Ergo-rondase	7 (13·2)	2·5	271 (264·8)	278
Totals ..	33		664	697

Chi-square=5·1. P less than 0·05. (Expected numbers in brackets.)

fusions were required, whereas 7 of the 32 controls lost more than 30 ounces and 2 required blood transfusion.

There was no significant difference between the numbers of secondary post-partum haemorrhages in each group.

MANUAL REMOVAL OF THE PLACENTA

The incidence of manual removal in the primigravidae was 0·9 per cent in the controls and 1·4 per cent in the Ergo-rondase group. In the multigravidae, 0·3 per cent of the controls and 0·4 per cent of the Ergo-rondase group required manual removal. These differences are not statistically significant.

There were, however, two differences between the control and the Ergo-rondase groups in relation to manual removal: (1) The average blood loss in cases of manual removal in the control group was 24·2 ounces, an amount almost twice as great as the average loss of 13·2 ounces in the Ergo-rondase cases; (2) the figures already given do not indicate a trend towards a greater number of manual removals in the Ergo-rondase group. The placenta was retained on 4 additional occasions, but was delivered by cord traction before induction of anaesthesia. If these cases are added to the true manual removals, the difference between the two groups is still not statistically significant, but there does seem to be a trend towards more cases of retained placenta in the Ergo-rondase group.

AVERAGE BLOOD LOSS

The data was re-examined after taking out all the cases of post-partum haemorrhage and of manual removal. In the case of the primigravidae the average blood loss in the controls exceeded that of the treated patients, the most important difference being that whereas 19·3 per cent of the controls lost more than half a pint (10 ounces) of blood, only 7·1 per cent of the Ergo-rondase cases lost more than this amount.

In the case of the multiparae, there was a trend towards a reduced average blood loss in the Ergo-rondase cases, but the difference between losses exceeding half a pint in the controls (14·6 per cent) and the Ergo-rondase group (12·9 per cent) is not statistically significant.

AVERAGE DURATION OF THE THIRD STAGE

There was good evidence that the Ergo-rondase treatment shortened the average duration of the third stage of labour. Thus, in the primigravidae, in 88·8 per cent of the Ergo-rondase cases, the third stage was completed within 10 minutes compared with 65·0 per cent of the normal controls.

Although the difference was not quite so marked in the multiparae, the trend was the same, thus in 88·5 per cent of the Ergo-rondase cases the third stage was completed within 10 minutes, compared with 77·2 per cent of the controls.

PUERPERAL ANAEMIA

In the control group, a post-partum haemorrhage or a manual removal complicated the third stage in 37 patients, 23 of whom (62·2 per cent) had a haemoglobin of 10 g. per cent or less after delivery. Of the 18 patients in the Ergo-rondase group who had third stage complications, 6 (33·3 per cent) were anaemic by the same standard. Thus, the incidence of anaemia in the controls was almost twice that of the treated group.

COMPLICATIONS

No local or general undesirable side-effects of the Ergo-rondase treatment were noted during the investigation. Although twin pregnancies were excluded from the survey, one case needs to be mentioned because Ergo-rondase was inadvertently administered during the birth. A gravida-3, who was known to have a twin pregnancy, was admitted at 34 weeks in the

second stage of labour. The midwife was unaware of the diagnosis and gave the Ergo-rondase injection with the birth of the anterior shoulder of the first baby which was then delivered. The uterus contracted frequently and strongly, did not relax completely between pains, and there was an intra-partum loss of 6 ounces of blood. The second foetal sac was ruptured artificially 15 minutes after the delivery of the first twin, and the second baby was delivered spontaneously by the vertex without further delay. This infant weighed 3 pounds 9 ounces, was deeply cyanosed at birth and respiration was never satisfactory. Death occurred after 10 hours. Autopsy showed asphyxial changes but no other lesion. The first baby weighed 3 pounds 12 ounces and caused no anxiety.

Flying Squad Cases

During the years 1949–1956, the City General Hospital Obstetric Emergency Service treated 106 patients in their own homes. Of these, 86 were primigravidae or gravidae 2–5 who were similar to the patients studied in hospital, and like them, developed unexpected third stage complications. The records of these cases were examined for data likely to be of value in this study. Of the 86 patients (36 primigravidae, 50 multigravidae), only 2 lost less than 30 ounces of blood; the average blood loss was 60·4 ounces and 69 blood transfusions were given. Many of these patients very nearly lost their lives.

Discussion

The results show that the incidence and severity of post-partum haemorrhage in a group of normal primigravidae, who were given an intramuscular injection of Ergo-rondase as a routine with the birth of the anterior shoulder, was significantly less than in a group of normal controls. In the case of normal multigravidae (gravidae 2–5), the incidence of post-partum haemorrhage was not reduced, but the severity of the bleeding was slightly less in the Ergo-rondase group. The average blood loss and the average duration of the third stage were reduced in the remaining Ergo-rondase cases, the difference being most marked in the primigravidae. The incidence of puerperal anaemia was greater in the control cases who had third stage complications than in the Ergo-rondase cases.

It is clear, therefore, that the greatest gains of the Ergo-rondase treatment were obtained in the primigravidae. So far as well-staffed hospitals are concerned, it is doubtful if the results obtained with the multiparae warrant the routine use of this empirical treatment. Further examination of the data is required to decide the value of the treatment in primigravidae.

There are two important issues to be discussed in order to clarify the position. Firstly, although there was a significant difference in the number of post-partum haemorrhages in the control and Ergo-rondase groups, the possibility that this difference was due to factors other than the Ergo-rondase has to be carefully considered. For instance, could the post-partum haemorrhage rate in the control groups have been reduced in any other way?

During the investigation, efforts were made to keep the number of third stage abnormalities in the control group as low as possible, but, despite this, the post-partum haemorrhage rate in the controls remained unaltered during the two years of the survey. The critical appraisal of the control group, far from encouraging the belief that many haemorrhages could have been avoided, indicated that the standard of care was of a very high order. For instance, emergency treatment was required for 15·3 per cent of the controls. Had the staff been less vigilant, more post-partum haemorrhages would have occurred. In contrast, the Ergo-rondase cases caused less anxiety and were much easier to manage, only 5·8 per cent requiring emergency treatment. After careful consideration it seems that the low incidence of post-partum haemorrhage in the treated group was due to the beneficial effects of the Ergo-rondase rather than to any other factor.

Secondly, are there any disadvantages to the Ergo-rondase treatment to offset the apparent advantages? There appears to be a potential danger to the second of undiagnosed twins. The neonatal death recorded in the present paper could, of course, have happened without the Ergo-rondase injection. Nevertheless, whatever the influence of the oxytocic on the outcome

of this case, it could not have been good. To justify the routine use of Ergo-rondase therapy, great care must be exercised to avoid this complication as far as possible and to deal efficiently with the rare mishap. The risk can be considerably reduced by withholding Ergo-rondase from cases of unexplained premature labour.

Martin and Dumoulin (1953), using prophylactic intravenous ergometrine, reported an increase in the manual removal rate. Although the substitution of a manual removal for a post-partum haemorrhage is generally acceptable, if routine prophylactic ergometrine therapy led to many manual removals in patients who would otherwise have been normal, the method would be unacceptable. In the present investigation, there was a slight trend in this direction, but this was offset by the use of cord traction in suitable cases. It may be that the decision to use routine ergometrine should coincide with a resolve to recognize the usefulness of cord traction, and to see that the house surgeons are properly instructed in its use.

No undesirable side-effects due to Ergo-rondase therapy were encountered in the present series, but allergic responses to hyaluronidase have been reported from time to time. Joubert (1957) has reported such a case in obstetrics. This risk is probably no greater than that of parenteral iron or blood transfusion—procedures frequently employed to restore patients who have had a post-partum haemorrhage.

The Ergo-rondase was not given to 121 normal cases as planned, a failure rate of 19·5 per cent. Such a high failure rate obviously diminishes the value of the method. The commonest reason was a rapid birth, the unassisted midwife being unable to manage to give the injection. The incidence of failures fell from 26·2 per cent in the first year to 13·5 per cent in the second year. Undoubtedly, the technique requires practice, but each midwife was almost 100 per cent successful after a few weeks. The relatively high failure rate was partly due to frequent staff changes.

Accordingly, there is a good case for recommending the routine intramuscular injection of ergometrine (0·5 mg.) and hyaluronidase (1 mg.) with the birth of the anterior shoulder in primigravidae. The method may deserve wider application in understaffed hospitals, but more evidence is needed. It will be recalled that the staff looking after the control cases were frequently required to deal with potential third stage abnormalities. It was felt that in less favourable circumstances, the post-partum haemorrhage rate would have been much greater. The outcome of such cases delivered at home is indicated by the work of the Obstetric Emergency Service. It is appreciated that the Flying Squad is generally only called out to the worst cases, but this does not alter the fact that such desperate cases are rarely seen following uncomplicated pregnancy and delivery in hospital. Kellar (1955) reported 66 deaths from post-partum haemorrhage in Scotland during 1949–54. Most of these deaths occurred in domiciliary practice, private nursing homes and small hospitals. Nixon (1957) has recently made a plea for the use of prophylactic ergometrine in domiciliary practice. It may be that the wider application of the Ergo-rondase method in home confinements (for both primigravidae and multigravidae) would be of considerable value. In this respect, the method has the virtue of being manageable by the unassisted midwife.

Summary

Intramuscular ergometrine (0·5 mg.) with hyaluronidase (1 mg.) was given to 500 selected normal patients in the second stage of labour with the birth of the anterior shoulder. The results were compared with those of 707 control cases.

The incidence of primary post-partum haemorrhage in primigravidae was significantly reduced from 6·2 per cent to 2·5 per cent. The incidence of post-partum haemorrhage in normal multigravidae (gravidae 2–5) was not reduced but the severity of the bleeding was less, as with the primigravidae.

The incidence of manual removal of the placenta was not significantly increased, but the blood loss in the treated group was reduced.

The average blood loss and average duration of the third stage in normal cases was reduced in the treated group.

Puerperal anaemia in the patients who had

abnormal third stages was less in the treated than in the control group.

The records of 86 patients treated by the Obstetric Emergency Service were reviewed.

It is concluded that the routine intramuscular injection of ergometrine (0·5 mg.) with hyaluronidase (1 mg.) given to normal hospital primigravidae is a worthwhile procedure. The method may also be applicable to multigravidae in understaffed hospitals. Wider use of the method in domiciliary practice is recommended.

Acknowledgments

I wish to express my sincere thanks to Professor C. S. Russell for allowing me to use his patients for this trial, and for his help in preparing the paper. Dr. W. J. Clancy kindly allowed his patients to be used as controls. The investigation would not have been possible without the co-operation of the house surgeons and the nursing staff, to whom I am most grateful.

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Obituary

KENNETH BOWES

M.D., M.S., F.R.C.S., F.R.C.O.G.

THE announcement of the recent death of Kenneth Bowes must have come as a great shock to many readers of this journal, for he was very widely known both in person and by his writings. To all who had met him sorrow would be added to shock. Of a retiring nature, Kenneth was the kindest of men and probably had not an enemy in the world.

His health had gradually deteriorated over recent years following two, or possibly three, attacks of infective hepatitis. In the last few months he must have felt definitely ill and he died in the early morning of Saturday, 1st February, six days after an abdominal operation.

The son of Dr. Joseph E. Bowes of Cumberland, Kenneth was educated at Queen Elizabeth's Grammar School, Blackburn, and at the University of Liverpool. How great were his abilities may be gauged by his academic successes. In 1929 he qualified M.B., Ch.B. (Liverpool), with 1st class honours and in the same year M.B., B.S. (London), also with honours. Two years later he was successful in the examination for the F.R.C.S. (Eng.) and in 1932 was awarded the M.S. and in 1935 the M.D., both of London University. In 1957 he was offered and accepted the Membership and Fellowship of the Royal College of Obstetricians and Gynaecologists.

He came to St. Thomas's in 1933, when he was appointed Surgical Registrar; two years later he decided that his life work was to be in Obstetrics and Gynaecology in which subjects he had previously been awarded the Gold Medal. He was successful in his application for the post of Registrar to the Department of Obstetrics and Gynaecology and from that time his course was clear and automatically he climbed the various steps on the ladder to the appointment of Surgeon to the Department in 1936. He was also consulting surgeon to the South West Metropolitan Regional Hospital Board. He was an external examiner for the University of Glasgow and had been examiner in Obstetrics and Gynaecology to the University of London and to the Conjoint Board.

Kenneth wrote easily and widely and well. His published work included contributions to all medical journals, to the *British Encyclopaedia of Medical Practice*, Hutchinson's *Index of Treatment*, Birch's *Treatment of Medical Emergencies*, and he was best known as Editor of *Modern Trends in Obstetrics and Gynaecology*. He died at the height of his career. His brilliant academic knowledge was backed up by good judgment as a clinician and by equal technical ability as a surgeon.

His tastes were of the simplest. He loved his home and all that goes with that wonderful word, and in it he would delight to entertain his many friends. Both he and his wife were perfect hosts. He never had any interest in games or sport, but was always happy pottering about in the garden of his house in the country near Guildford. He was never a robust man as he had had a very severe illness in his boyhood and there is no doubt that throughout his life there were many times when he kept going only by great effort and determination. A member of the Gynaecological Club, he always looked forward to and thoroughly enjoyed every visit and meeting.

Kenneth had the kindest disposition. He probably thought ill of no one; he certainly never spoke ill of anyone. He was always ready to help no matter how pressing was another

engagement nor how tired he might be. He possessed a great and keen sense of humour—so keen that most people only saw the point of some remark long after he had vanished.

It is not out of place to record the judgment of one of his house officers, who told me "Mr. Bowes moves in a mysterious way his wonders to perform". This particular man had had continual difficulty in reaching the ward before his chief had been round all his cases and had disappeared. Doubtless Kenneth's reply to the Sister or Nurse who asked whether she should send for Mr. So-and-so was usually "Oh no, I don't think there is any need to trouble him". He did not seem to realize at all how greatly the residents and the students valued his teaching.

The most gentle of men, he was held in the greatest affection by all of us who knew him. He can never be replaced.

A. J. WRIGLEY.

THIRD WORLD CONGRESS ON FERTILITY AND STERILITY

AMSTERDAM, 7TH TO 13TH JUNE, 1959

THE Third World Congress on Fertility and Sterility, sponsored by the International Fertility Association, will be held in Amsterdam, Holland, from 7th to 13th June, 1959.

The general outlines of the sections of the programme will be as follows:

(1) Female sterility (Physiology of reproduction, pathology, endocrinology, clinical problems, treatment).

(2) Male sterility (Physiology of reproduction, pathology, endocrinology, clinical problems, treatment).

(3) Basic research and/or animal reproduction.

(4) Psycho-sexual problems.

Titles for papers should be sent not later than June, 1958, to both Dr. Alfonso Alvarez-Bravo, Avenida Horacio 1506, Mexico City 5, D.F., Mexico, chairman, and Professor Dr. B. S. ten Berge, Academisch Ziekenhuis, Groningen, Holland, executive member of the Programme Committee.

For further information and registration apply to Dr. L. I. Swaab, Hon. Secretary, Third World Congress on Fertility and Sterility, Sint Agnietenstraat 4, Amsterdam-C., or to the nearest Wagons Lits/Cook office.

SECOND WORLD CONGRESS OF THE INTERNATIONAL FEDERATION OF GYNAECOLOGY AND OBSTETRICS

THE Second World Congress of the International Federation of Gynaecology and Obstetrics, which will be held in the newly-built Queen Elizabeth Hotel in Montreal, Canada, from 22nd to 28th June, 1958, will have on its programme eight main lectures given by eminent scientists whose studies and research are related to the field of gynaecology and obstetrics. The guest speakers and the title of their lectures are as follows:

Professor Murray L. Barr, Department of Microscopic Anatomy, University of Western Ontario, London, Canada.

"Tests of Chromosomal Sex and Their Application to Clinical Problems"

Professor Hermann Bautzmann, Anatomisches Institut, Hamburg, Germany.

"Comparative Studies on the Histology and Function of Animal and Human Amnion"

Professor Roberto Caldeyro-Barcia, Chief of the Section of Obstetrical Physiology, Faculty of Medicine, Montevideo, Uruguay.

"Contractility of the Human Gravid Uterus and its Application to the Obstetrical Clinic"

Professor G. W. Harris, Head of the Department of Neuroendocrinology, Maudsley Hospital, London, England.

"Relationship of the Central Nervous System to Pituitary and Reproductive Activity"

Professor Charles Oberling, Institut de Recherches sur le Cancer Gustave Roussy, Villejuif (Seine), France.

"The Cytology of the Cancerous Cell"

Professor Bradley M. Patten, Chairman, Department of Anatomy, University of Michigan Medical School, Ann Arbor, Michigan.

"The Establishing of Foetal–Maternal Vascular Relations"

Professor Hans Selye, Director of the Institute on Experimental Medicine and Surgery, University of Montreal, Montreal, Canada.

"Stress in Gynaecology"

A representative of the U.R.S.S. (on a subject of his choice).

All correspondence should be directed to the Montreal Committee, Second World Congress, International Federation of Gynaecology and Obstetrics, 1414 Drummond Street, Suite 220, Montreal 25, Canada.

REPORTS OF SOCIETIES

GLASGOW OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

October 1957

A meeting of the Glasgow Obstetrical and Gynaecological Society was held in the rooms of the Royal Faculty of Physicians and Surgeons, Glasgow, on Wednesday, 16th October, 1957. The President, Professor D. F. Anderson, was in the Chair.

Dr. C. J. Mackinlay addressed the Society on

Ovarian Tumours

He said that it was obvious that only a small portion of such a vast subject could be dealt with in one lecture. Two questions had particularly interested him in the pathology of ovarian tumours. The first question was why were so many ovarian tumours adenomatous when the ovary itself contained no glands! One might expect to see fibromas or sarcomas but during the period 1948–53 there had been diagnosed in the laboratory of the Royal Samaritan Hospital for Women, 18 papillary serous cysts, 108 pseudomucinous cysts and 57 adenocarcinomas all of which were adenomatous tumours as against 27 fibromas. He considered that simple serous cysts should be excluded as the majority of them were not neoplastic and that dermoids were a separate group. He thought that the answer to this question lay in the nature of the ovarian stroma which was a highly specialized tissue. He likened the ovarian stroma to a cocktail in that one could not tell from its appearance what its effect would be but, if one knew the ingredients, one had a fair idea of its potentialities.

He then proceeded to remind his audience of some of the salient features of the embryology of the gonad. In his opinion, the sex cords were developed from the coelomic epithelium and developed in the male into the seminiferous tubules, a process which was accompenied by the appearance of Leydig cells in the interstitial tissue. He thought that the Sertoli cells which formed the seminiferous tubules were oestrogen secretors and essentially female cells and that the Leydig cells were androgen secretors and were essentially male cells. The reason for the very large number of Leydig cells in the foetal testis was that they were required to maintain the maleness of the foetus against the oestrogens produced by its own testis and the maternal oestrogens.

He admitted that this was an over-simplification but it struck him as a reasonable explanation. In the developing ovary the sex cords lost their radial pattern and became scattered through the ovary, losing their epithelial appearance but not their potentiality and merged with the mesenchyme to form the stroma. Some of the sex cords became pre-granulosa and later granulosa and produced Graafian follicles. He thought that the marked thecalutein reaction round developing follicles in the foetus was a parallel to the development of Leydig cells in the interstitial tissue of the testis.

The ingredients of the stroma were the derivatives of the coelomic epithelium and the stroma would therefore retain some of the potentialities of the coelomic epithelium. The coelomic epithelium lined the Müllerian duct and differentiated into tubal epithelium, endometrium, cervical epithelium and the squamous epithelium of the portio vaginalis and part of the vagina. If the coelomic epithelium went into a resting phase, as it appeared to do in the ovarian stroma, it still retained an enormous potentiality. If stimulated to form a tumour it was not surprising that the stroma should reproduce cells which the coelomic epithelium was normally capable of forming. This would explain the similarity between the cells of the cervix and those of the pseudomucinous cyst and the cells of the tube and those of the papillary serous cyst. He thought that many of the cases of endometriosis arose in a similar way but the friability of the endometrial cyst prevented the formation of large cystic tumours. In malignant tumours, he indicated that the papillary serous adenocarcinomas was much commoner than the pseudomucinous cyst-adenocarcinoma, a reversal of the ratio in simple tumours and was at a loss to explain this anomaly. Most of the carcinomas, however, were, for want of a better name, called primary adenocarcinomas. He thought that the primary adenocarcinomas might be related to the endometrium as there was quite a similarity between this type of carcinoma and endometrial adenocarcinoma.

The second question which had interested the lecturer was what was the difference, if any, between the granulosa cell tumour and the arrhenoblastoma and why should one kind of tumour be masculinizing and the other femininizing? He pointed out that, in Meyer's original series of 20 arrhenoblastomas, only 3 were definitely masculinizing but a number of these tumours looked to him like granulosa cell tumours. He then described a series of 34 functioning ovarian tumours from the Royal Samaritan Hospital for Women which he divided histologically into 3 groups; thecomas, diffuse granulosa cell tumours and differentiated granulosa cell tumours. He illustrated how the granulosa in these tumours appeared to be able to differentiate either towards a luteal or Leydig type of cell, which he considered to be a move in a more male direction, or towards a Sertoli type of cell-forming cords, an adenomatous pattern or tubules which were very similar to the seminiferous tubules of the foetal testis. The Sertoli cell-pattern was frequently accompanied by the appearance of luteal or Leydig cells in the surrounding granulosa or connective tissue. He interpreted the appearance of these cells as an attempt on the part of the tumour

to preserve the oestrogen-androgen balance. The clinical effect of these tumours depended not on the number of cells in the tumour which were capable of producing oestrogen or androgen but on the amount of hormone which was actually being produced. He thought that Meyer was wrong in calling arrhenoblastomas tumours of male precursors because the precursor seemed to be the granulosa. The tubularity of an arrhenoblastoma had no relationship to its capacity to produce masculinization. This capacity was due to the luteal or Leydig cells which the arrhenoblastoma contained. He thought, therefore, that much confusion would be avoided if the terms arrhenoblastoma, androblastoma and gynandroblastoma were discarded and the degree and direction (luteum or Sertoli) of the granulosa cell tumours were described.

The lecture was profusely illustrated by means of photographs.

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

October 1957

A Meeting of the North of England Obstetrical and Gynaecological Society was held in Liverpool on 18th October, 1957. The President, Mr. F. Stabler, was in the Chair.

Drs. J. E. Forster and H. H. Francis read a paper on

Pregnancy in Addison's Disease

A case of pregnancy in Addison's Disease, in which Caesarean section was required, was described. The management was given in detail. Transient exophthalmos and lid retraction in the baby thought to be due to the administration of cortisone to the mother immediately before delivery was recorded. Evidence of enhanced fertility due to cortisone treatment was presented and as a result it was suggested that the number of patients with Addison's Disease and pregnancy was likely to increase.

Discussion

The President commented on the rareness of the condition, but, as with diabetes, more of these cases may arise in future. He was interested in the small size of the child, and the problem of intra-uterine death at the 36th week of pregnancy. Usually the placenta was normal, but perhaps there were changes in the decidua, and with more prolonged cortisone therapy these changes might be improved.

Mr. J. G. Wigley described a patient who at first pursued a normal course. Following the removal of a thyroid tumour recovery was not satisfactory, and later she became pregnant. She had hyperemesis and was thought to be neurotic as only hypotension was found. After removing to Chester there was rapid improvement and labour and delivery were normal. Twelve hours after delivery she noticed weakness which increased for the next 3 to 4 days, when a diagnosis of Addison's disease was established and treatment commenced. In a subsequent pregnancy, pigmentation was noticed, and there was marked improvement in the patient's health in the last month, perhaps because of foetal suprarenal activity.

Dr. J. Forster said that on hydrocortisone many of these patients looked very well, but they were on the edge of a crisis, which could be precipitated by influenza or pregnancy. They required glucose as well as saline, and at the time of delivery a mineralocorticoid.

Mr. H. R. Arthur read a short paper on

A Survey of Eclampsia in the North-East of England

One of the main reasons for the present report is that the most comprehensive clinical survey of the problem of eclampsia was presented to the British Congress of Obstetricians and Gynaecologists as long ago as 1922. Since then an impression has grown that eclampsia is becoming less frequent and less severe, and it was felt that a fresh survey would be instructive. A particular area was selected, and a detailed analysis of the incidence of eclampsia during the 20-year period 1931–1950 was undertaken. This area consisted of Northumberland and Durham excluding Darlington and Stockton-on-Tees, both of which are outside the region of the obstetrical service centred on Newcastle. The population includes industrial Tyneside, the coalfields of Durham and Northumberland, and a wide agricultural area: approximately 2½ million people.

An analysis has been made of the 634 cases of eclampsia admitted to the Princess Mary Maternity Hospital and 483 cases admitted to other institutions: a total of 1,116 cases. Cases of fits in which there was any doubt of the true diagnosis were excluded.

In 1931 the incidence of eclampsia in the Princess Mary Maternity Hospital was 2·03 per cent of all admissions, and in 1950 it had fallen to 0·63 per cent, though the total annual admissions have not varied. Over the whole area, however, the incidence of eclampsia has remained constant. In other regions, where additional obstetric accommodation has been opened, there has been a decline in the incidence of eclampsia at the main hospital.

Despite economic depression, economic recovery, war, and the post-war years it is clear that there has been no significant change in the annual incidence of eclampsia in the period under review. As hospital records probably represent a reasonably accurate figure for the total number of cases in the area, the overall incidence is calculated at 0·14 per cent (1,116 cases of eclampsia in 786,259 total births). This finding of a maintained incidence of eclampsia is in direct opposition to opinions expressed on both sides of the Atlantic.

The mortality from eclampsia has fallen in the main hospital from 20·0 per cent (1931) to 0 per cent (1950), and in the North-East area in the same years from 21·4 per cent to 3·8 per cent. Similarly there has been an improved foetal mortality with figures falling from 65 per cent to 25 per cent. There have been a number of reviews of eclampsia from widely separated clinics, and these

show a uniform improvement despite a variety of treatments, the most dramatic improvement being in the decade 1940–1950.

This improvement in mortality is apparent in all the different institutions. If the type of treatment is not wholly responsible for the reduced death rate, then it may be that either the cases are less severe, or that the response to treatment is better.

In considering the clinical pattern of eclampsia it was only possible to use the series of 634 cases from the Princess Mary Maternity Hospital. The relationship to age and parity remained constant in the years under review; eclampsia is commoner in the 20–30 age group and in primigravidae. Eclampsia in later years was more frequent in the later weeks of pregnancy, and more cases occurred in labour and post-partum. Also, as shown by the number of fits, less than half as many patients can be classified as severe in the years 1946–1950 as in the years 1931 to 1935, and the number of patients having 5 or more fits before admission to hospital and the institution of treatment also decreased. In 1922 Eden laid down a standard of severity for eclampsia. By this standard 43·5 per cent of cases in the years 1931 to 1935 were severe, and in the years 1946 to 1950 27·9 per cent.

In the early years the number of patients discharged from hospital without residual hypertension or albuminuria was 8 per cent, but more recently this figure has risen to 50 per cent, the improvement commencing in 1935, 5 years before there was any radical change in treatment. It is justifiable, therefore, to say that in the North-East Region the cases of eclampsia admitted to the main hospital show a change in the clinical manifestations, and have become less severe.

The social class, economic level of the population and marriage rate appeared to have no influence on the incidence or severity of eclampsia. Unemployment and full employment also showed no marked effect. Density of population revealed the highest rate in semi-urban Durham and rural Northumberland, and when calculated against total birth rate rural Northumberland showed a percentage incidence 3 times higher than the rest of the area. Finally, there is no doubt that, while the survey indicates that the prognosis of eclampsia has improved, it also illustrates Professor Morris's words: a diminishing incidence of eclampsia requires closely knit maternity services and a really adequate antenatal accommodation. And the latter, alas, is not by any means entirely in the hands of the clinicians.

Discussion

The President thanked Mr. Arthur for his exposition. He had had the impression that eclampsia had decreased at the Princess Mary Maternity Hospital, but antenatal care has lamentably failed to reduce the incidence in the whole area. He was not sure if there was a real reduction in the severity, but that some forms of harmful treatment had been abandoned.

Mr. S. B. Herd asked if the increasing numbers of post-partum cases were severe or mild.

Dr. E. A. Gerrard compared the incidence of eclampsia in Manchester and Dublin, and thought the quality of the antenatal care and the matter of defaulters of importance.

Mr. H. H. Francis enquired if the Flying Squad had contributed to earlier treatment.

Mr. T. F. Redman raised the consideration of Hamblin's figures. If there was no antenatal bed, it was better to send a postnatal patient home early.

In reply Mr. Arthur said that he had the impression the postnatal cases were not so severe. They usually were already in hospital, and controlled at once. The Flying Squad had not been much used for this purpose. With meticulous antenatal care and an adequate provision of hospital beds then the incidence of eclampsia could be reduced.

Mr. T. B. FitzGerald read a paper on

THE REPAIR OF RECTO-VAGINAL INJURIES

(This article appears on page 296 of this issue)

Discussion

The President had observed that the superficial part of the external sphincter usually tore at 3 or 9 o'clock.

Mr. H. R. Arthur asked if the new muscle remained active after operation.

Professor C. S. Russell preferred a low residue diet just after this type of operation.

Mr. H. H. Francis advocated a detergent to keep the faeces soft. He also commented on the disdain with which the sphincter is treated in fissure and fistula operations.

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

NOVEMBER 1957

A Meeting of the North of England Obstetrical and Gynaecological Society was held in Manchester on 15th November, 1957. The President, Mr. F. Stabler, was in the Chair.

Mr. P. C. Steptoe reported a case of

MALIGNANT ADENOMYOSIS UTERI

During the 4 years 1952 to 1955, 4,590 gynaecological cases were admitted to the hospitals in the area. Of these, 210 patients had a malignant neoplasm: an incidence of 4·4 per cent.

The patient under review was seen first in July, 1954 at the age of 37 complaining of heavy irregular periods, a brown discharge, and post-coital bleeding for 8 months. She showed moderate anaemia, her haemoglobin being 44 per cent, and on vaginal examination the uterus was found to be enlarged and there was a small cervical polypus.

Blood transfusion was given prior to operation. The uterine cavity was found enlarged apparently by a submucous myoma, and curettage revealed no naked eye suspicion of malignancy. A total hysterectomy with conservation of both ovaries was performed. Examination of the uterus confirmed the presence of a small fibroid

and also showed areas of adenomyosis. Section from one of these areas showed the appearance of benign adenomyosis, but in a further section the glands appeared malignant.

The patient's general condition remained good until December, 1954, when she complained of lower abdominal discomfort, and a cystic, tender mass attached to the vault of the vagina was found. At laparotomy both ovaries were cystic, and after freeing adhesions bilateral salpingo-oöphorectomy was done. Section of the ovaries showed no evidence of malignant deposits, but one cyst suggested endometriosis.

In September, 1956 a tender firm mass was found attached to the vaginal vault. This nodule, 1½ inches in diameter, was removed, and on section showed the presence of endometriosis in a muscular stroma. No further symptoms or abnormal signs have since been found at frequent visits.

There is very little reference in the literature to carcinoma associated with adenomyosis, though stromal malignancy is described.

Discussion

The President was intrigued how seldom malignant change was found in ectopic endometrium. He was uncertain if the malignant appearance could be accepted in this case.

Mr. H. Malkin accepted that the section showed adenocarcinoma, but thought the malignancy might have arisen in the endometrium.

Mr. L. Snaith asked if the nodule removed at the third operation had been present earlier on.

Professor C. S. Russell commented on the continued oestrogen stimulus after removal of the ovaries and suprarenals, but perhaps the different types of oestrogens have different actions.

Professor T. N. A. Jeffcoate was doubtful as to the evidence of malignancy. If this was accepted it could not be said that the subsequent nodule was malignant. It was very unusual to find both intra-uterine and extra-uterine endometriosis, and therefore, if the extra-uterine endometriosis was proved, the uterine tumour was an adenocarcinoma arising in the endometrium.

Mr. Steptoe in reply said that three pathologists were unanimous that the uterine tissue was malignant. The nodule removed at the third operation had not been found at earlier operations or at several examinations.

Mr. T. F. Redman read a short paper on

The Significance of Some Unusual Foetal Cardiac Arrhythmias

(This article appears on page 304 of this issue)

Discussion

The President thought that these foetal cardiac irregularities might be commoner if sought after. The bradycardia is sometimes temporary, and he asked if Mr. Redman was referring to this type of case, or the one in which the foetal heart remained slow for some days.

Professor W. I. C. Morris mentioned the difficulties of foetal electrocardiographs, and even of auscultatory signs. With a rate over 140 it is difficult to be sure the irregularity is due to premature beats, and one must be hesitant about making a precise diagnosis.

Mr. C. J. Dewhurst reported a case in which the foetal heart had been rapid and at intervals falling to 100. The patient, after reading her notes, decided against active intervention, and a normal delivery followed. The baby's heart rate remained irregular for 4 weeks, but is now normal.

Dr. R. Newton hoped that a machine could be devised for recording the foetal heart. He had had a similar experience to Mr. Dewhurst. A Caesarean section was done, and the baby died 4 years later from congenital heart disease.

Mr. T. B. FitzGerald thought there was no need to be discouraged. He had a machine and it produced very complicated tracings.

Mr. Redman, in reply, said that in some instances the abnormality persisted throughout labour, and after delivery electrocardiograms had been done. It was not possible to confirm partial heart block before delivery.

Mr. G. Trevor Johnson read a paper on

The Course of Pregnancy Complicated by Essential Hypertension

Pregnancy which is complicated by essential hypertension has gained a sinister reputation for the high loss of foetal life with which it is associated. At the Princess Mary Maternity Hospital in the years 1955 and 1956 there were 4,122 births of which 104 were from 103 mothers with essential hypertension. The diagnosis was based on a resting blood pressure of 140/90 mm. mercury on two or more occasions before the 20th week of pregnancy. The majority of these patients had booked early in pregnancy, only 11 were emergency admissions, 36 were primigravidae, and 69 multiparae ranging between their 2nd to 11th pregnancies. Fertility was poor in patients with essential hypertension and an average of 6 years had elapsed since marriage in comparison with 2 years in the normotensive group.

Pre-eclampsia was the most striking antenatal complication. It occurred in 54 per cent of the patients which was more than 4 times the local incidence, and it was noted as early as the 26th week of pregnancy though more usually in the last 4 weeks. Accidental haemorrhage occurred in only 4 cases.

The 103 mothers gave a history of 262 pregnancies of which one-fifth had ended in abortion or perinatal death, and a further fifth of the infants weighed 5½ pounds or less at birth. Their present pregnancies resulted in 104 infants with 21 premature births and 14 perinatal deaths. The maternal risk was considerable; one mother died from concurrent tuberculous meningitis and more than half sustained a further rise in blood pressure.

The vasospasm occurring in hypertension results in tissue ischaemia and arteriosclerosis, and within the decidua this lessens the capacity for placental development. Pre-eclampsia has a similar effect, and the combination of both conditions is particularly hazardous.

Eleven of the 14 perinatal deaths occurred in patients with added pre-eclampsia.

Of the small number of patients developing pre-eclampsia before the 30th week, 75 per cent lost their babies, but during the last month only 10 per cent of the babies died. The severity of the pre-eclampsia was also ominous.

It is generally agreed that foetal survival is proportional to the severity of the hypertension in early pregnancy. The present series is small, but if the diastolic pressure exceeded 110 mm. mercury before the 20th week the birth weight was two-thirds that of babies born to mothers with diastolic pressure of 90 mm. mercury. A fall in diastolic blood pressure in the middle weeks of pregnancy also coincided with heavier birth weights.

There were 37 patients exceeding 35 years, and the mean birthweight of their babies was 1 pound less than the younger age group, and stillbirths 3 times more common.

The present problem is to decide at which stage of pregnancy foetal demands outstrip its limited placental capacity, and then to rescue the infant from its anoxic environment by prompt delivery. The passage of minute amounts of radio isotopes can be traced from maternal to foetal tissues, and 5 millilitres normal saline labelled with 20 micro-ounces Na^{24} is most suitable for this purpose. Placental function can be compared in normal and abnormal pregnancies. The records of 2 patients with hypertension were shown. The first, a primigravida of 22 years also showed early renal failure and a raised blood urea. The uterus grew proportionately, but at the 37th week a reduction in placental function was definite. Caesarean section resulted in a live child. In the second case, a previous child had been lost, but repeated estimations of placental function spared the need for interruption of the pregnancy.

In conclusion, essential hypertension results in delay in achieving a pregnancy, an increased foetal loss due to abortion and perinatal death, and in increase in the number of premature infants. A more favourable prognosis was found with a lower diastolic blood pressure and those cases in which there was a fall in blood pressure in the middle weeks of pregnancy.

Discussion

The President congratulated Mr. Johnson on the work he had done. He mentioned how difficult it was to draw conclusions as to the management of these cases of hypertension. In one the uterus failed to grow normally, but in another with the same level of hypertension foetal growth was normal, He thought that hypertension was unaffected by pregnancy.

Mr. T. F. Redman asked if the labile type of high blood pressure was more serious than the constant hypertension, and to what extent the induction of labour has influenced the incidence of premature babies.

Mr. J. M. Gate found that the foetal loss reported by Professor Browne was not in agreement with the 91 per cent foetal survival in this part of the country. Moreover he had found the average weight of babies born to hypertensive mothers only 2 ounces less than those born to normotensive mothers. In his cases a high incidence of Caesarean sections had avoided some stillbirths.

Mr. T. B. FitzGerald was very interested in those cases in which the baby fails to grow. He recognized 2 types of foetal death: one in which there was placental failure, and the other associated with accidental haemorrhage. Should it be found that the baby is not growing, expectant treatment should be abandoned and Caesarean section done.

Professor C. S. Russell supported this view in cases of failure of the baby to grow. It was this type of case that had prompted pregnanediol excretion estimations, and usually a low excretion was found with clear evidence of placental insufficiency.

Mr. C. J. Dewhurst commented on the reduced fertility in hypertensive patients, and wondered if they waited longer and therefore were more liable to hypertension. He was also concerned about the total dose of irradiation.

Professor W. I. C. Morris thought one point had not been sufficiently stressed. On the whole essential hypertension is extraordinarily benign. When the systolic blood pressure was less than 160 mm. mercury the outlook for the babies was better than for all patients. For more severe cases, there were a few in which poor foetal results occurred, and Mr. Johnson had shown one way in which these cases could be picked out.

In reply, Mr. Johnson said that the maximum amount of irradiation equalled that given at the time of a single X-ray of the pelvis. The prognosis for the foetus was better in the cases with a labile blood pressure, and concurrent pre-eclampsia may be the cause of foetal death in the last weeks of pregnancy.

THE EAST ANGLIAN OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

November 1957

The temporary petrol rationing had caused the postponement of our March meeting until 2nd November, 1957, when we met at Addenbrooke's Hospital, Cambridge, under the Chairmanship of our President, Mr. Bulman.

Mr. T. J. Ryan read the opening paper on

The Use of the Pitocin Drip in Obstetrics

Mr. Ryan based his report on his experience in the use of this technique on 355 patients at the Western General Hospital, Edinburgh, and subsequently on 106 maternity patients at Cambridge Maternity Hospital. He recognized three groups of cases where the use of a pitocin drip was advisable.

Indications

(1) Those women whose membranes have been ruptured either spontaneously or artificially for 24 hours and in whom labour has not begun.

(2) Those women in whom induction of labour is associated with some degree of urgency, for example those with severe pre-eclampsia, eclampsia, concealed acci-

dental haemorrhage. In these patients artificial rupture of the membranes should be immediately followed by the administration of a pitocin drip.

(3) Uterine inertia. Patients who have been in labour for 24 hours and in whom the inertia is of the hypotonic type often benefit greatly from the administration of a pitocin drip.

Method

One quarter ml. (2·5 units) of pitocin is *thoroughly* mixed with one bottle (540 ml.) of dextrose, dextrose in saline, or normal saline alone. The drip needle is inserted into a vein just above the wrist, occasionally on the back of the hand, and rarely in the ante-cubital fossa. If the last site is avoided, a splint will seldom be required. This allows the patient to move her arm and herself about while the drip is running, thus preventing most of the discomfort usually associated with a drip.

The drip is commenced at a rate between 40 and 80 drops per minute and is allowed to run without these limits *until at least the end of the first stage*. There is no attempt to alter the rate unless it falls to below 40 or rises above 80 drops per minute. These wide limits are allowed on the reasoning that a drip cannot be kept at a fixed rate for any length of time.

Constant supervision of the patient is *not* carried out and the foetal heart is not checked more frequently than is customary during labour.

N.B.—There is a 50 per cent failure if the membranes are not ruptured.

Results

The onset of labour was very rarely delayed more than 12 hours, and in only 8 cases did it fail to start. These patients were delivered by Caesarean section. There were no maternal deaths in the series and in no instance did the uterus rupture. One stillbirth was attributable to the method.

He has used a pitocin drip to induce labour in cases of ante-partum haemorrhage, pre-eclampsia and eclampsia, disproportion, multiple pregnancy, and in cases of labour following a previous Caesarean section.

Discussion

Mr. Bulman still regarded pitocin as a dangerous drug and considered that its slight vaso-pressor activity might precipitate an eclamptic fit in cases of severe pre-eclampsia.

Mr. Lloyd admitted that Mr. Ryan had converted him from his previous scepticism to enthusiasm for the method. When he was in the U.S.A. recently he found that pitocin drips were being used extensively to induce labour, largely for reasons of convenience.

Mr. O'Meara stated that he still remained staunchly conservative in his use of oxytocic drugs.

Miss Bottomley drew attention to the flexibility of the technique as the drip could be readily stopped at any time the obstetrician thought advisable.

Mr. Bruce Eton believed that syntocinon (Sandoz) would be safer as it was free from vaso-pressor activity.

Mr. Stansfield considered that the technique had a place in modern obstetrics provided that the mother was closely supervised throughout the labour and this meant noting the foetal heart rate and the type of uterine contractions every 15 minutes. He would require to know the results obtained in 2 to 3 thousand cases before advising extensive use of a pitocin drip.

Mr. Carlisle favoured the use of a pitocin drip to induce labour, but he restricted the use of any form of induction. He reported one case of death from a *E. coli* peritonitis following induction of labour.

Mr. MacKenzie reported that he was using the pitocin drip to induce labour, but he always stopped it when labour started.

Mr. Bulman summed up the feeling of the meeting by saying that we could accept the innovation with many restrictions on its use.

The next paper was read by Mr. Bruce Eton on

The Results of the Treatment of Carcinoma of the Body of the Uterus

A series of 189 cases of endometrial carcinoma have been reviewed in collaboration with the Radiotherapeutic Centre and the Pathological Department of Addenbrooke's Hospital, Cambridge. The results were assessed in 163 cases traced. One hundred and nine patients were followed up for 5 years and showed a relative cure-rate of 63·3 per cent. This differs little from the absolute cure-rate as only one patient was untreated. About one-third of the patients treated were aged between 65 and 84 years.

In the cases where the extent of the growth had been recorded, a comparison was made between the 5-year cure-rate for primary surgery in 52 patients (59·6 per cent) and primary surgery plus irradiation in 26 patients (65·4 per cent). The difference may be significant if one considers that the post-operative irradiation was probably given in the more advanced cases, or in cases where there was special reason to fear the possibility of subsequent vaginal vault metastases.

Six patients were treated with radiotherapy only in spite of the fact that the growth was confined to the uterus, because they were bad operative risks. As none of these survived 5 years it would seem that some of them ought to have been given a chance with surgery.

It is true that in most cases a cure can be obtained by simple total hysterectomy and removal of the adnexa. It is equally true that in many cases the condition is so far advanced that no kind of treatment is likely to cure the patient. It is in the remaining cases where we might find scope for improvement.

It is felt that there may be a place for giving pre-operative radium a trial. The Manchester type of insertion of an intra-uterine applicator and two vaginal applicators in the lateral fornices for the treatment of the parametrium should be tried for a length of time which would have to be advised by the radiotherapist. Treatment would be given for 3 or 4 days, so that a cancer-lethal dose could be delivered to a significant volume of tissue.

We will take X-ray films in order to enable the physicist to calculate the distribution of radiation and we will measure the dosage of radiation delivered to the rectum when the radium is in position. If the cervix is involved, a larger dose of radium treatment will precede the operation.

A few days later total hysterectomy and removal of the adnexa will be carried out, the extent of the operation depending on the individual case.

Advanced cases and those unfit for surgery will be treated by Heyman's applicators, using a single insertion technique to deliver 5,000 to 5,500 r. to a distance of 0·5 cm. from the outline of the radium as shown on X-ray.

Cases which are too advanced for curative treatment are to be treated by means of deep X-ray therapy only.

Discussion

Mr. Bulman felt that we must all be dissatisfied with our results in the treatment of carcinoma of the uterus. In patients suffering from carcinoma of the body of the uterus we were hampered by the concurrence of old age and obesity with malignant disease. He personally was afraid to use radium pre-operatively because of the risk of disseminating the growth by the trauma of the insertion of radium, and because it is impossible to assess the depth of invasion of the growth and the consequent danger of causing extensive necrosis.

Miss Bottomley reported that she had used radium according to Heyman's technique for the bad operative risk patients. This method had its particular difficulties and dangers. In one case it produced a pelvic abscess.

Mr. Kimbell stated that he had treated 35 cases since 1952. After confirmation of the type and site of the carcinoma by fractional curettage, the patient was treated with radium. Fifteen milligrammes of radium were placed in the utero-cervical canal and 20 milligrammes in each lateral fornix and left there for 72 hours. Three to 4 days later a total hysterectomy was performed. It was too early yet to report 5-year cures.

Mr. Stansfield was of the opinion that carcinoma of the body of the uterus should be divided into two groups.

(1) Carcinoma of the fundus.

(2) Carcinoma extending to the internal os.

The first group received pre-operative radium followed in 14 days by a total hysterectomy using precautions against spill of uterine contents. The second group required radium therapy and this was followed in 14 days by a Wertheim's hysterectomy. The radium was applied in a catheter loaded with 10 to 12 five milligramme radium needles. This was coiled up in spiral fashion in the body of the uterus and left in place for 72 hours. It was too early to report his results. The difficulty in making any change in treating cases of carcinoma was the delay of ten years before one could determine the results.

Mr. Awona had studied the sugar metabolism in cases of climacteric bleeding. Fifty of his patients were suffering from carcinoma of the body of the uterus and 4 of these had abnormal glucose tolerance tests. Two were known to be suffering from diabetes mellitus. He advocated a hysterectomy in cases of climacteric bleeding where the sugar metabolism was abnormal. This might forestall the development of carcinoma of the body of the uterus.

Mr. Bulman summed up the discussion.

There was no unanimity of opinion as to the best treatment for carcinoma of the body of the uterus. Should radiation be used at all? If so, when and in what form, and how soon should surgery be used? We still were without an answer to these questions.

Miss J. E. Bottomley reported

FOUR CASES OF ENDOMETRIOSIS IN UNUSUAL SITUATIONS

Microscopic slides of endometriosis in the appendix, groin, and umbilicus were shown.

Mr. M. W. B. Bulman described a case of

MALIGNANT MELANOMA OF THE FACE ASSOCIATED WITH EARLY PREGNANCY

He asked the advice of the members on the treatment of this patient for his colleague Mrs. Townsley. The consensus of opinion was that the pregnancy should be terminated on the grounds that gestation probably accelerated the growth of melanoblasts.

BOOK REVIEWS

"The Gynecological Management of Urologic Injuries." By HENRY C. FALK. Pp. 265. 97 illustrations. F. A. Davis Company, Philadelphia, 1957. Price $7.50.

THIS is one of the well-known series of obstetrical and gynaecological monographs issued by Davis and Company of Philadelphia. It is an excellently produced and lavishly illustrated volume.

Dr. Henry C. Falk, who is one of the leading New York gynaecologists, has produced an essentially practical book in which he clearly describes his own practice and experience. His succinct text is necessarily dogmatic and personal but, where appropriate, reference is made to the methods successfully employed by other workers. The first and largest section contains an excellent account of the treatment of vesico-vaginal fistulae; the next deals with stress incontinence of urine; and the third concerns the management of ureteral injuries.

There is much to commend and little to criticize. The section on vesico-vaginal fistulae deals exclusively with vaginal methods of repair. For post-hysterectomy cases the Latsko technique (high colpocleisis involving the vaginal vault only) is advocated; and it is interesting to note that the author is so confident of the repair that he dispenses (in this type of case) with the usual post-operative bladder drainage. Due attention is accorded to vesico-cervical fistulae, and to fistulae following Caesarean section; a special chapter is devoted to the management of cases in which there is complete loss of the urethra. The Schuchardt incision is described and depicted. Many gynaecologists will question, however, whether this "savage" cut is necessary—least of all in its double form—save on the rarest of occasions; far oftener a simple, midline episiotomy will give all the extra access that is needed.

The section on stress incontinence of urine describes methods similar to those generally used in this country. Various types of case are distinguished—those suitable for vaginal operative procedures; those for which a sling operation is better fitted (Studdiford's modification of the Aldridge operation is favoured); and those for which the Marshall Marchetti operation can well be used. These various procedures are each considered in detail. Some of the vaginal methods (short of the complete "Manchester" operation) are unusual, and will be noted with interest.

The ample section on ureteric injuries is especially welcome for this important subject is too often omitted, or glossed over in a few words, in many gynaecological textbooks.

This is a really useful publication which can be warmly commended to gynaecologists in this country.

J. Chassar Moir

"Anatomy of the Trigonum Vesicae and the Aetiology and Treatment of Spontaneous and Traumatic Obstetrical Urogenital Fistulae." By D. A. E. NOREL. Pp. xii+239, with 19 figures. Dekker and Van de Vegt N.V., the Netherlands, 1956. (In English, with summaries in English, Dutch and French.)

THIS publication is difficult to classify and assess. It contains a vast amount of information on bladder injuries, and includes appendages on the anatomy and embryology of the urinary tract. A large part of the book is a painstaking collection of relevant world literature, with more than 400 publications listed in 17 pages of titles.

The author, Dr. Norel, was formerly Chief of Service in Surgery and Gynaecology in the Military and Government Hospital of Bobo-Dioulasso in French West Africa; and much of her work concerned the treatment of vesico-vaginal fistulae following prolonged or difficult labour. She describes many methods of repair and supplements these with numerous case histories.

To anyone already well versed in this class of work, Dr. Norel's book will be of value not only because of the author's undoubted experience but also because of the abundant information which she gives concerning the methods of other workers both past and present. (Unfortunately, these are not always quoted with complete accuracy.) For the inexperienced worker this book cannot be recommended. The wealth of detail is such that the reader cannot, at times "see the wood for the trees".

J. Chassar Moir

"Suprapubic Closure of Vesicovaginal Fistula." By VINCENT J. O'CONOR, Professor and Head of Department of Urology, N.W. Medical School, Chicago. Pp. xi+53, with 9 figures. Charles C. Thomas, Springfield, Ill., and Blackwell Scientific Publications, Oxford, 1957. Price 20*s*.

THIS booklet concerns the treatment and case records of 33 patients with high vesico-vaginal fistulae.

After a brief historical introduction and a listing of possible methods of operation, the author at once proceeds to the detailed description of one particular operation. This is an abdominal exposure of the bladder, a midline bisection of that organ backwards to the fistula site, the excision of the fistula by a "racquet-shaped incision", the re-suture of the bladder, and the provision of suprapubic drainage.

This is an already established technique, and Dr. O'Conor refers to the descriptions given in several of the standard British textbooks of urology. The present

publication is however remarkable for its clear text, the numerous excellent illustrations, and the detailed case histories. Twenty-nine of 31 patients treated were completely cured by the procedure described.

While this abdominal method of repair can in many cases give very satisfactory results it is, as Dr. O'Conor acknowledges, associated with difficulties and dangers of its own. Thus, it may be far from easy to gain access to the under surface of the bladder; nor can the considerable risk of injuring the ureters be ignored when, as is often the case, they are caught up in scar tissue around the fistula. Gynaecologists may well wonder whether the difficulties that are sometimes encountered in the vaginal repair of fistulae are not exchanged for equal or even greater difficulties when the abdominal approach is used. Be this as it may, this booklet is a very useful addition to surgical literature, and one that should be carefully studied by gynaecologists and urologists alike. The price seems rather high.

J. Chassar Moir

REVIEW OF CURRENT LITERATURE

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ANATOMY, PHYSIOLOGY

89. Experimental and Morphological Studies of the Blood Supply to the Ovaries. (Experimentelle und morphologische Untersuchungen zur Erforschung der Blutversorgung der Eierstöcke.)

By GY. GYÖRGY, J. LASZLO and L. FEHER. *Zbl. Gynäk.*, **79**, 1867–1877. 1957. 10 figs. 22 refs.

In the experimental part of this work one ovary was removed from virgin does. The hilum of the other ovary was stimulated *in situ* with an electric current of 5 volt. This resulted in a naked-eye dilatation of the hilar vessels, engorgement of the superficial capillaries and enlargement of the whole ovary. A similar change could be produced by stimulating the cervix or the vagina, or by mechanical stimulation of the vagina with a small metal rod. These reactions failed to take place if the lumbo-dorsal part of the spinal cord was severed. Histological examination of ovaries which had shown the reaction confirmed the hyperaemia of the arteries, capillaries and veins.

The authors demonstrated the presence of flaps bulging into the lumen of the larger veins of the rete ovarii and cushion-like projections in the smaller veins, in which non-myelinated nerve-fibres end in club-shaped terminals. These structures suggest an independent mechanism of closure in the veins. Similar findings were made in human ovaries, at all ages between infancy and menopause.

The authors believe that in addition to the already known mechanism by which the degree of arterial dilatation and arteriovenous shunts determine the ovarian blood supply, there exists a second mechanism of closure in the ovarian venous system. Both would contribute to the rapid changes taking place in the ovary of the rabbit, leading to active and passive hyperaemia and, possibly, ovulation.

[The article is well illustrated.]

Bruce Eton

90. A Radiological and Obstetrical Survey of the Female Pelvis.

By C.-E. JOHANSON-UNNÉRUS. *Acta obstet. gynec. scand.*, **36**, Suppl. 8. 1957. 14 figs. bibliography.

This monograph of 91 pages is a report on a radiological study of 1,099 women of various ages and parity, representing a cross-section of the Finnish female population. Subjects with obvious pathological features were excluded. The series is made up of 480 nulliparae, 224 primiparae, and 395 multiparae. An age classification with five-year limits was made in order to study the age incidence of possible changes. In addition 100 pregnant women were examined.

Both with increasing parity and with increasing age the pelvis gradually becomes flatter and broader; it is the true conjugate that undergoes a significant change. The sacrum becomes more curved or horizontal in position

with both increasing age and increasing parity. The sub-pubic angle increases with parity, and decreases at the time of the menopause. During pregnancy, both the sagittal and the transverse diameter of the mid-pelvis and the sub-pubic angle increase; after delivery there is no complete return to the ante-partum state.

The author's series, which was obtained at the gynaecological clinics of Helsinki University, included a higher proportion of android and platypelloid pelves than the series of other investigators. His radiological studies also proved the inadequacy of external pelvic measurements as a basis for the estimation of internal measurements.

N. Alders

91. **Urinary Excretion of the Serotonin-Catabolite 5-Hydroxy-indolyl-3-acetic Acid (HIES) During the Normal Menstrual Cycle.** (Über die Ausscheidung des Serotonin-Kataboliten, 5-Hydroxy-indolyl-3-essigsaure, im Urin während des normalen Zyklus.)

By F. ROTH and R. RICHTER. *Zbl. Gynäk.*, **79**, 1733–1740. 1957. 1 table. 2 figs. 62 refs.

The physiological significance of serotonin in the living organism is not yet clear. Pharmacologically it acts on smooth muscle of the blood vessels and hollow organs, especially the uterus. It has an anti-diuretic effect on the kidney by inhibiting both water and chloride excretion.

It seems that only a third of the circulating free serotonin appears as 5-hydroxy-indolyl-3-acetic acid (HIES) in the urine. Bearing this in mind, the authors estimated the daily HIES excretion per 24 hours throughout six complete menstrual cycles in 5 healthy volunteers. The amounts excreted per 24 hours varied between 0 mg. and 6·1 mg., with an average of 1·74 mg. There were considerable variations during any one cycle, but there was a significant maximal excretion shortly before and on the first day of menstruation. The possible causes of this rise may be an increase in the catabolism of serotonin in the blood, or blockage of further dissimilation of HIES, or an increased direct breakdown of 5-hydroxy-tryptophan to HIES. If the greater output at the onset of menstruation corresponds to a rise in serotonin, it may be responsible for the increase in physiological contractions of the uterus, and through its vaso-constrictor action, may be concerned with the mechanism of uterine haemostasis.

Bruce Eton

PREGNANCY

92. **Total Exchangeable Sodium and Space in Normal and Pre-eclamptic Patients Determined with Sodium^{22}.**

By W. J. DIECKMANN and R. POTTINGER. *Amer. J. Obstet. Gynec.*, **74**, 816–833. Oct. 1957. 8 tables. 6 figs. 15 refs.

Using sodium^{22}, which has a longer half life of 3 years compared with 14·8 hours for sodium^{24}, the authors have followed its metabolism in over 170 non-pregnant, normally pregnant and pre-eclamptic subjects and also studied the last two groups in the puerperium. The results show that both sodium space and exchangeable sodium are increased in normal pregnancy, and markedly increased in pre-eclamptic patients, as evidenced by a 32 per cent drop by the 8th post-partum day.

F. J. Browne

93. **An Experimental Inquiry Into the Etiology of Pre-eclamptic and Eclamptic Toxemias. A Preliminary Report.**

By F. H. HOWARD. *West. J. Surg. Obstet. Gynec.*, **65**, 370–371. Nov.-Dec. 1957. 5 refs.

The author attempted to demonstrate a toxic factor in amniotic fluid by precipitin reactions between the liquor and sera of patients suffering from pre-eclampsia. Twenty-two patients seem to have been examined and in the words of the author "these experiments can only lead to speculation".

D. C. A. Bevis

94. **The Use of Protoveratrine in Pre-Eclampsia.** (De toepassing van protoveratrine by zwangerschapstoxicosen.)

By A. SIKKEL and J. WOLFF. *Nederl. Tijdschr. Verlosk. Gynaec.*, **5**, 459–479. 1957. 6 tables. 4 figs. 30 refs.

The authors report the experience gained during 1956 with protoveratrine in Prof. van Bouwdijk Bastiaanse's clinic in Amsterdam. A protoveratrine preparation, Puroverine (Sandoz), was given orally, intramuscularly or intravenously to 31 patients with severe pre-eclampsia. Ten of these were suffering from pre-eclampsia only, the remainder having the disease superimposed on an essential hypertension. One of these had a severe essential hypertension with minimal pre-eclampsia and showed no response to the drug. The remaining 20 patients with essential hypertension and superimposed toxaemia showed an average fall of 40 mg. Hg in systolic and 20 mm. Hg in diastolic blood pressure. Patients with pure pre-eclampsia showed an average fall of 35 mm. Hg systolic and 25 mm. Hg diastolic pressure. In all cases the amount of albumen in the urine declined. The perinatal deaths numbered 4 out of 31 babies. All the deaths occurred in markedly premature infants.

Nausea and vomiting occurred in many cases but responded to aluminium hydroxide and phenobarbitone. Vascular symptoms resulting from a rapid fall in blood pressure were controlled with ephedrine hydrochloride and bradycardia was treated with atropine sulphate. No evidence of foetal damage by protoveratrine was found but it is somewhat alarming to note that slowing of the foetal heart was found in some cases of maternal bradycardia, suggesting that the alkaloid does cross the placental barrier. The authors conclude that there is a good indication for the use of this drug where it is necessary to allow the pregnancy to continue for a few weeks in order to obtain a viable baby.

Arnold Klopper

95. **Severe Haemorrhage due to Afibrinogenaemia in a Case of Eclampsia.** (Schwere Defibrinierungsblutung und Eklampsie.)

By P. WILLE. *Zbl. Gynäk.*, **79**, 1740–1749. 1957. 2 tables. 2 figs. 132 refs.

The author reports the case of a gravida-2 who, after

delivery of a live child, suffered uncontrollable haemorrhage. The diagnosis of afibrinogenaemia was made eventually but, in spite of blood transfusion, the patient died, apparently as a result of irreversible shock and uterine atony. Post-mortem examination showed numerous sub-capsular haemorrhages in the liver and eclamptic liver necrosis. There had been no signs of eclampsia before delivery.

The author discusses the possible relationship between acute afibrinogenaemia and eclampsia, the latter being attributable to multiple emboli of fibrin in the cerebral arterioles. However, in most cases of eclampsia there is no afibrinogenaemia. In fact, there is more often evidence of an increase in the coagulability of the blood of toxaemic patients.

[This case again raises the question whether the pathological changes found in the liver of these patients are in fact pathognomonic of eclampsia.]

Bruce Eton

96. **Treatment with Anticoagulants of Pregnant Women with Previous Severe Toxaemia.**

By J. Løvset, K. Knutsen and A. Jakobsen. *Acta obstet. gynec. scand.*, **36**, 492–498. 1957. 4 figs. 16 refs.

This is a short report, coming from Bergen (Norway), on the prophylactic use of anticoagulants in a series of 12 pregnant women who had lost a total of 16 infants between the 24th and 40th weeks of previous pregnancies, due to pre-eclamptic toxaemia. All these 12 women gave birth to living, and surviving, infants weighing between 2,508 and 4,000 g. None of the mothers developed severe toxaemia, and no complications due to the anticoagulant therapy were observed.

[Although this series is too small to allow of optimism, which might be premature, this line of thought, ultimately based on James Young's theory of partial placental infarction and necrosis as a cause of pre-eclamptic toxaemia, may be worth following. It must be borne in mind, however, that the patients treated with anticoagulants (no details about the treatment and prothrombin index estimation are given in this paper) were almost certainly admitted to hospital and given suitable diet whilst under treatment.]

N. Alders

97. **A Carbonic Anhydrase Inhibitor for Control of Fluid Retention in Pregnancy.**

By C. C. Briscoe. *Obstet. Gynec.*, **10**, 251–260. Sept. 1957. 6 figs. 37 refs.

There is some evidence that the oedema of pregnancy toxaemia is associated with a sodium-retaining factor which is a highly active mineralocorticoid other than desoxycorticosterone. Acetazoleamide (Diamox) is a carbonic anhydrase inhibitor and, as such, acts as a powerful diuretic, producing loss of water, sodium, and potassium. It is possible in pregnancy to control weight gain due to retention of fluid by intermittent or continuous administration of acetazoleamide, for months if necessary. Prolonged administration does not lower the serum levels of $Na+$, $K+$ or $Cl-$, although a metabolic, symptomless acidosis develops.

The drug has been effective in preventing the accumulation of fluid even in the presence of a high intake of sodium.

J. G. Dumoulin

98. **New Methods of Treatment of Threatened Abortion and Premature Labour.** (Neue Wege in der Behandlung der drohenden Abortus und Frühgeburten.)

By B. Zsolnai and I. Nyiri. *Zbl. Gynäk.*, **79**, 1800–1811. 1957. 2 tables. 2 figs. 22 refs.

The authors base their study on the following known facts. During pregnancy an increase occurs in the body of acetylcholine and histamine, both of which are concerned with uterine motility. The uterus is also influenced by the nervous system. Chlorpromazine has a depressant effect on both the sympathetic and parasympathetic nervous systems.

Preliminary *in vitro* and *in vivo* experiments carried out by the authors in pregnant and non-pregnant animals showed that largactil and phenergan reduce uterine contractions produced by acetylcholine, histamine and oxytocin.

In their clinical trial they compared the results of treatment with largactil in a series of 98 cases of threatened abortion and premature labour with 238 controls treated by conventional methods. Pregnancy was conserved in 67 per cent of the former compared with 48 per cent of the controls. The threat of abortion or premature labour was diagnosed if the patient had bleeding or painful contractions.

In patients with a history of habitual (more than 3) abortions 7 pregnancies out of 8 were saved with largactil compared with 6 out of 14 of the controls.

The authors conclude that largactil is a useful addition to the treatment of threatened abortion and premature labour, because it acts as a central sedative, it reduces uterine tone and inhibits the action of the autonomic nerves on the uterus. If it is true that allergic factors may be responsible for habitual abortion, the use of largactil as an antihistamine drug would seem rational.

It is admitted that in many cases where the ovum is faulty or the chorio-decidual relations are seriously damaged, largactil would be of no value.

Bruce Eton

99. **Pregnancy and Coarctation of the Aorta.**

By J. F. Goodwin. *Lancet*, **1**, 16–20. Jan. 4, 1958. 2 figs. 28 refs.

In cases of coarctation without pregnancy, the majority of patients die before 40 years of age. Twenty-five per cent of the patients die from aortic rupture or dissection; 25 per cent from bacterial endo-aortitis and endocarditis; 25 per cent from congestive heart failure; about 10 per cent from cerebral vascular accidents; and 15 per cent from other causes. Cardiac lesions confer the added hazards of bacterial infection and heart-failure. Hypertension is rarely severe and although the systolic pressure may be high, the pressure is extremely labile. The author reviews 136 cases of pregnancy and coarctation of the aorta. The mortality in this series was 9·5 per cent and probably does not exceed that of coarctation alone. The

two commonest single causes were aortic rupture and aortic aneurysm, and heart failure was found only when cardiac lesions were also present. The observations lead to the conclusion that pregnancy does not confer an added risk to patients with uncomplicated coarctation, but the presence of added heart disease may radically alter the position because of the hazards of heart failure and bacterial endocarditis. Hence during pregnancy very careful watch must be kept for signs of aortic infection and of aortic aneurysm. Active chemotherapy and resection of the coarctation may be indicated. When there is additional serious heart disease, the diagnosis must be made early so that pregnancy can be terminated before the 20th week. If the pregnancy has progressed further the management should be as for any other patient with heart disease and pregnancy.

[No definite reason is given why the 20th week of pregnancy is chosen as the dividing line.]

H. H. Fouracre Barns

100. **Pregnancy and Delivery After Bilateral Adrenalectomy for Cushing's Syndrome.**

By G. T. SCHNEIDER, J. C. WEED and C. Y. BOWERS. *Obstet. Gynec.*, **10**, 437–443. Oct. 1957. 4 figs. 10 refs.

Cushing's syndrome is uncommon and most patients who have it are sterile. Since 1945, 15 patients (14 of them women in the child-bearing age) with Cushing's syndrome were treated at the Ochsner Clinic, New Orleans, Louisiana. The course of pregnancy after adrenalectomy was followed in 3 cases. In 1 case, the adrenalectomy was subtotal: in this, the pregnancy and delivery were uneventful, requiring no steroid therapy.

The 2 cases of total adrenalectomy with subsequent pregnancy are described in detail. The first of these became pregnant 2½ months after operation. She was receiving 250 mg. hydrocortisone acetate every 2 weeks intramuscularly (changed to weekly for the rest of the pregnancy) and 2 g. of sodium chloride daily. Her antenatal course was uncomplicated. Extra hydrocortisone was given during labour which was uneventful and the treatment was gradually reduced post-partum.

The second patient conceived 1½ years after operation when on a daily oral dose of cortisone 25 mg. This was increased to 37·5 mg. There were no complications in this case either.

Recent work suggests that there is no significant foetal or placental steroid support during pregnancy.

J. G. Dumoulin

101. **Liver Cirrhosis and Pregnancy: Report of a Case Following Spleno-Renal Shunt.**

By J. ADNO. *S. Afr. med. J.*, **31**, 1189–1191. Nov. 23, 1957. 9 refs.

Pregnancy associated with hepatic cirrhosis or severe liver disease is a very infrequent occurrence. The literature is reviewed and the danger of haematemesis is stressed.

A case is presented in which 2 pregnancies occurred after spleno-renal shunt in a patient with Banti's disease. During the second pregnancy at 25 weeks she threatened to abort and showed oedema. Serum sodium was low, and she was given a high salt intake with disappearance of the pains, and later the oedema.

It is thought that infertility in patients with severe hepatic disease is due to associated endocrine and general metabolic upset.

If patients with cirrhosis seem to be in good health and well compensated there is no indication for termination of pregnancy, although some cases have associated varices and unexpected haematemesis. The latter is due to increased pressure in the portal system as the abdominal cavity is filled by the growing pregnancy. A diet high in protein and rich in carbohydrate should be prescribed. Any deterioration in the patient's condition should be assessed with a view to termination. The author favours strict bed rest in the later stages and awaits spontaneous labour which is assisted with the forceps. Caesarean section should be performed only for obstetrical reasons and when rapid termination is required. The presence of oesophageal varices contraindicates future pregnancies.

L. J. Abramowitz

102. **Candidal Cystitis in Pregnancy: Report of Two Cases.**

By H. ANNAMUNTHODO and J. H. M. PINKERTON. *Obstet. Gynec.*, **10**, 428–431. Oct. 1957. 26 refs.

Two cases of cystitis associated with pregnancy and due to *Candida albicans* are described. Each had a haemorrhagic type of cystitis which was extremely difficult to treat. Neither had had previous antibiotic treatment but both had a candidal vaginitis and this was thought to be the source of infection.

The condition tends to be severe and very painful. It is chronic and may be exacerbated by antibiotic therapy. Various treatments have been suggested such as bladder irrigation with borax, silver nitrate or gentian violet. Therapy in the two cases described was not very successful, but both recovered spontaneously after delivery.

J. G. Dumoulin

103. **Pregnancy During Hodgkin's Disease.**

By C. M. SOUTHERN, H. D. DIAMOND and L. F. CRAVEN. *Cancer*, **9**, 1141–1146. Nov.-Dec. 1956. 3 tables. 12 refs.

Fifty-nine patients are reviewed in this paper. They had between them 83 pregnancies concurrent with Hodgkin's disease. The survival rate was shorter in those patients who first manifested the disease during pregnancy than in those who entered pregnancy with established disease. The prognosis was best in the group of patients where the disease had been inactive for at least 9 months prior to conception. Spontaneous abortion was commonest in patients with intra-abdominal or widespread disease. No ill effects on live born children were observed.

The authors state that whilst pregnancy is undesirable in Hodgkin's disease the study permits no conclusion as to whether or not therapeutic abortion is of any value.

S. Way

104. **Carcinoma In Situ of the Human Uterine Cervix in Pregnancy: Prevalence and Post-pregnancy Persistence.** By M. MARSH and P. J. FITZGERALD. *Cancer*, **9**, 1195–1207. Nov.-Dec. 1956. 8 tables. 13 figs. 15 refs.

Among 3,970 patients in 4,067 pregnancies biopsy showed 2 invasive carcinomas (0·05 per cent) and 20 intra-epithelial carcinomas (0·49 per cent). The prevalence increased with age from the twenties through the early forties. Seven of the 20 patients were followed up with biopsies from 13 to 31 months after delivery and in all the lesion persisted. The authors believe that any clear-cut lesion which experienced observers would call intra-epithelial carcinoma will persist after delivery, and conclude that the assessment of the lesion in pregnancy does not differ from that in the non-pregnant.

S. Way

105. **Endometriosis and Pregnancy.** (Endometriosis genital y embarazo.)

By J. C. AHUMADA, J. L. SARDI and L. A. ARRIGHI. *Obstet. Ginec. lat.-amer.*, **15**, 15–26. 1957. 65 refs.

A series of 467 cases of endometriosis found at operation, in which only 17 patients had achieved pregnancy, is reported. Of 221 of these patients in whom the endometriosis was present in the uterine cavity, only two were pregnant. The authors point out that such cases at term are especially prone to complications such as rupture of the uterus if forceps are applied, whilst uterine atonia and post-partum haemorrhage could easily occur. Peritoneal or ovarian endometriosis with ectopic pregnancy was not found, and they state that according to the literature, it is extremely rare. On the other hand, in a series of 50 cases of tubal endometriosis, 12 ectopic pregnancies were discovered. The nearer the endometriosis is situated to the abdominal ostium of the Fallopian tube, the greater is the incidence of ectopic pregnancy. Three other cases were found in association with endometriosis in the recto-vaginal pouch, a situation which does not impair fertility.

Studying the histology of these cases, the authors found that the endometriosis tissue proliferates during pregnancy and shrinks again afterwards. Decidual reaction occurs, which almost gives it a malignant appearance.

John F. Foulkes

106. **Association of Pregnancy and Endometriosis.** By H. FREDRIKSON. *Acta obstet. gynec. scand.*, **36**, 481–491. 1957. 3 figs. 15 refs.

The author reports 9 histologically verified cases of this rare combination from Gothenburg (Sweden) University.

In 8 cases there was ovarian endometriosis with or without endometrial implants on the pelvic peritoneum. Two patients underwent operative removal of ovarian endometrial cysts during the second month of pregnancy, the pre-operative diagnoses being ovarian cyst and ectopic pregnancy respectively; both patients were delivered of living children at term. Two patients aborted spontaneously, at the 8th and 13th week of pregnancy respectively, and laparotomy confirmed the pre-operative diagnosis of ovarian endometriosis in both cases. One patient underwent laparotomy for the removal of a large, necrotic uterine fibroid, 2 months after a normal delivery; endometrial cysts were found in both ovaries, and because of their size were considered to have been present during the preceding pregnancy. In one patient bilateral ovarian endometrial cysts were found during Caesarean section at the 8th month. The remaining 2 cases were of a tubal pregnancy with endometriosis in the ovary of the same side, and of a primary ovarian pregnancy implanted into a true endometrial lesion of the ovary, respectively.

The ninth case was one of endometriosis situated in the posterior vaginal fornix and increasing during pregnancy in size from that of half a walnut to that of a hen's egg; the patient was delivered with forceps at term.

N. Alders

107. **Pubic Chip-Fracture: Report of Two Cases Occurring During Pregnancy and Labor.** By M. FRAENKEL and M. SALZBERGER. *Obstet. Gynec.*, **10**, 393–396. Oct. 1957. 6 figs. 8 refs.

Two cases of spontaneous fractures of bony particles, chip-fractures, from the symphysis pubis are reported. One occurred in the latter part of pregnancy, and the other immediately following delivery. In order to determine the frequency of this lesion a series of 250 consecutive radiograms of the symphyses of women before delivery was reviewed. This revealed 2 cases with X-ray findings resembling those in the 2 reported cases, but with no history of pain. A further 500 radiograms of non-pregnant women aged 20–30 did not reveal similar findings.

J. G. Dumoulin

LABOUR

108. **Axial Rotation of the Uterus as a Cause of Dystocia.** (Rotación axial uterina como factor de distocia.)

By A. F. ORTIZ. *Obstet. Ginec. lat.-amer.*, **15**, 43–47. 1957. 30 refs.

The author reports a case of rotation of the uterus to an angle of 90°, in which a Caesarean section had to be performed to end a protracted labour, during which foetal distress developed.

The patient was a primigravida aged 22 years. After 19 hours of strong labour, with the membranes ruptured, the foetal head remained unengaged, and the cervix was only one finger dilated. Foetal distress occurred, and Caesarean section was therefore undertaken. Upon opening the abdomen by a mid-line sub-umbilical incision, the left round ligament and vessels of the left broad ligament immediately came into view. Exploration of the peritoneal cavity revealed adhesions present at the right aspect of the lower uterine segment, so that the uterus had been rotated during its expansion through an angle of 90° with the pelvic axis. By the lower segment procedure, a live baby was extracted.

The author could not find a similar case in the literature.

John F. Foulkes

109. **Refined Relaxin and Length of Labor: A Preliminary Report.**

By C. H. Birnberg and M. M. Abitbol. *Obstet. Gynec.*, **10**, 366–370. Oct. 1957. 4 tables. 5 refs.

Relaxin, a substance isolated from pregnant sow ovaries, was described by Hisaw in 1926 (*Proc. Soc. exp. Biol., N.Y.*, **23**, 661). Animal experiments show that it softens the cervix. The authors used a purified form "Cervilaxin" on 200 women in labour. They claim that when combined with oxytocin the length of labour is reduced by a half or more of that achieved with oxytocin alone provided the following conditions are met: (*a*) the membranes are ruptured, (*b*) the cervix is at least 75 per cent effaced and 3 cm. dilated, and (*c*) adequate uterine contractions are present.

Cervilaxin alone produces a marked softening of the cervix. *J. G. Dumoulin*

110. **Experiences with the Vacuum Extractor, with Special Reference to the Indications for its Use.** (Erfahrungen mit dem Vakuumextraktor in der Geburtshilfe unter besonderer Berücksichtigung der Indikationsstellung.)

By H. Meinrenken and W. Scheiferstein. *Geburtsh. u. Frauenheilk.*, **17**, 1086–1096. Dec. 1957. 4 tables. 28 refs.

The authors have analyzed the results obtained using the suction-tractor, described by Malmström and Uddenberg, at the University Gynaecological Clinic of Cologne. The article is prefaced by an interesting historical description of the development of this method of delivery.

The results of operative deliveries undertaken during 2 periods of 10 months before and after the introduction of the vacuum extractor are compared. The total number of deliveries in each period was 1,250 and 1,423, respectively. The number of Caesarean sections was 50 and 52 and the number of forceps deliveries was 36 and 29, respectively. The suction-tractor was used on 61 occasions during the second 10-month period. The authors have used this method of delivery mainly as a supplementary obstetric aid rather than as a substitute for the forceps.

The indications for using the vacuum extractor were, uterine inertia 30 times and foetal distress on 21 occasions. The remaining indications were placenta praevia, prolapse of the umbilical cord, pre-eclampsia, etc.

There was no difference in the maternal mortality or morbidity rates in the 2 groups. The foetal mortality rate was 16·7 per cent and 15·1 per cent in the two 10-monthly periods. The incidence of birth injuries was 29·6 per cent in those babies delivered by the suction-tractor as compared with 3·1 per cent in those babies delivered by forceps. The foetal morbidity was increased the longer traction was maintained.

The authors state that the advantages of this instrument are that it can be used during the first and second stages of labour and that general anaesthesia can be dispensed with. In view of the risk of injury to the foetus they do not recommend substituting the suction-tractor for the forceps, but would limit its use to cases of primary or secondary uterine inertia or foetal distress. There is little place for the use of the instrument in the delivery of deflexed heads or other malpresentations.

Peter J. Huntingford

111. **Fetopelvic Grading of Breech Presentations.**

By D. F. Kaltreider. *J. Amer. med. Ass.*, **165**, 132–135. Sept. 14, 1957.

The incidence of breech presentation at the University of Maryland Hospital over a period of six years from 1950 to 1956 was 3·34 per cent. The overall perinatal loss was 23·3 per cent. The corrected loss in service patients was 2·3 per cent and in private patients 0 per cent. The author suggests methods of improving the overall figures by better obstetric practice rather than by statistical corrections.

The decision between vaginal delivery and Caesarean section depends upon three factors. These are (1) pelvic size, (2) pelvic shape, and (3) estimated foetal weight. Full X-ray pelvimetry decides the pelvic size and shape, and a true conjugate of less than 10 cm. contraindicates vaginal delivery unless the foetus is premature. The areas at the plane of the inlet, the interspinous level, and the anteroposterior diameter of the outlet are estimated by the method described by Mengert, and after considering the general shape (the flat pelvis and the small android type are particularly unfavourable) a system of pelvic grading is presented. There are eight grades, and a pelvis graded between 5 and 8 usually indicates Caesarean section. The foetal weight is estimated by having four or more examiners give an estimate without the knowledge of others and averaging the estimates. In addition to these mechanical factors the action of the uterus must also be taken into account. *D. W. James*

112. **The Management of Breech Presentation.**

By L. W. Cox. *N.Z. med. J.*, **56**, 370–384. Aug. 1957. 5 tables. 6 figs. 52 refs.

This paper begins with a series of tables showing the mortality for uncomplicated breech delivery, from many hospitals and also in personal series. With trained obstetricians (personal results) the foetal mortality was between 0·8 and 2·9 per cent. In hospital series it was between 0·9 and 9·9 per cent. The author suggests that other unpublished results may not be as good as these. The foetal mortality in reported series for cephalic version varies between 0·7 and 5·9 per cent. Once again the fallacy is exposed that breech presentation in multigravidae is not dangerous.

In the hands of some obstetricians the mortality from breech delivery is very low, while in the hands of others the mortality from cephalic version is very low. It is suggested that the individual obstetrician should choose his own method for the particular case. It is emphasized that the management of breech presentation should be in the hands of trained obstetricians, since a general practitioner, even one with a very large practice, cannot attend enough breech cases to become proficient. It is only by referring and concentrating these cases, that good results can be attained.

The remainder of the article deals with the diagnosis of breech presentation, the management of labour, and the

delivery of the breech, according to the method of Burns and Marshall. *From the Author's Abstract*

113. **Saddle Block Anesthesia in Breech Delivery.**
By H. I. DAILY and S. M. ROGERS. *Surg. Gynec. Obstet.*, **105**, 630–634. Nov. 1957. 3 figs. 3 refs.

The authors report a series of 486 breech births of infants weighing over 1,000 grams during the period 1952 to 1956. Of these 169 were delivered under saddle block anaesthesia. The block was given in the 3rd and 4th lumbar interspace, with the patient sitting up for a period of precisely 30 seconds. The agent used was 4 mg. of pontocaine in 2 ml. of 10 per cent dextrose and was administered when the breech was visible at the perineum. It was considered to be an excellent anaesthetic for assisted breech delivery (partial breech extraction) but not for complete breech extraction when deep general anaesthesia is required.

There were no maternal complications in this series attributable to the use of saddle block anaesthesia nor could it be held responsible for any of the infant deaths.

The authors conclude that saddle block anaesthesia is the equal of any known type of anaesthesia for assisted breech delivery and that it does not deserve the condemnation which it has received in the past.
John P. Erksine

114. **Manual Removal of the Placenta Without General Anaesthesia.**
By H. J. H. CLAASSENS. *S. Afr. med. J.*, **31**, 1147–1150. Nov. 9, 1957. 1 table. 10 refs.

The author presents 102 cases in which manual removal of the placenta was performed without general anaesthesia. He maintains that the procedure was safe, easy and in some cases probably life-saving. The fear of sepsis need no longer be a deterrent factor whether an anaesthetic is used or not. Shock may be due to haemorrhage, Crédé's manœuvre, anaesthesia, blood transfusion complications or retained placenta. The dangers and difficulties of anaesthesia are discussed.

The technique employed is described. Morphine gr. ¼ was given intravenously, although it is suggested that gr. 1/6 should suffice. Daptazole was never indicated. Shock was treated by blood transfusion. It was not necessary to wait until the blood pressure had reached 100 mm. Hg, as long as it was rising with anti-shock treatment.

The complications were hour-glass constriction in 29 cases, all of which yielded to amyl nitrite, a morbidity rate of 9 per cent and apprehension in a few patients. Only 6 of 72 patients felt that the pain was worse than that of childbirth. *L. J. Abramowitz*

LACTATION, PUERPERIUM

115. **The Iron Content of Human Milk in Relation to Iron Therapy.** (Valori siderimetrici del latte materno e trattamento marziale.)
By A. FABIANO. *Ann. Ostet. Ginec.*, **78**, 1043. Oct. 1956. 72 refs.

Studies have been made on the iron content of human milk during the puerperium. It is found that there is a progressive diminution in the iron content of milk between the second and the eighth day of the puerperium. The iron content on the first day of the puerperium is higher than that of milk obtained at the end of the first week. This is probably due to the higher mineral content of colostrum than of milk. The elimination of iron in colostrum is higher in primiparae than in multiparae.

A constant and progressive diminution in the iron content of human milk takes place during the second, third, fourth and fifth months after delivery.

Administration of iron to puerperal women leads to increase in the daily elimination of iron in the milk. This reaches a peak at about the seventh day of the puerperium. This increase is more marked in primiparae than in multiparae.

There is a case for the administration of iron to lactating women as a way of improving the iron supplies of the newborn infant. *Josephine Barnes*

116. **A Sulphonamide Mixture Which Passes Freely Through the Placenta.** (Studio sperimentale sul passagio dal sangue materno al sangue fetale di una nuaova sulfa-associazione: il Dosulfin o G.21815.)
By L. BRUNO, *Minerva ginec., Torino*, **9**, 608–610. July 31, 1957. 2 tables. 20 refs.

A mixture of sulphonamides often appears to be more effective than one particular compound. The author has tested one called Dosulfin which is a mixture of sulphamerazine and "G.14289", which has been reported as being particularly safe and effective for all the usual infections susceptible to sulpha treatment, including some due to viruses, and to be free from unpleasant or harmful effects. It is also less liable to the risk of producing resistant strains than the penicillin series. The standard dose is 3 g. daily.

Two grammes of the drug were administered to 30 women early in labour, and on its completion maternal and foetal blood were tested for free and combined "dosulfin". In all cases the amount in the foetal blood was nearly identical with that of the mother, and it was also present 24 hours later in the foetal urine. Concentrations in maternal blood averaged 3·63 and 4·44 mg. per cent ml., free and total respectively; the corresponding figures for the foetus being 3·47 and 4·27 mg. per cent. No ill effects were noted.

[It would be interesting to know the percentage in the liquor amnii. As sulphamerazine is not thought to be altogether safe in certain dosages, some other sulphonamide mixture might be safer. Sulphonamides in general are stated to pass the placental barrier without difficulty.]
W. C. Spackman

117. **Clinical Observations on the Passage of Radioactive Iodine (I 131) through the Human Mammary Gland.** (Osservazioni cliniche sul passagio dello jodio radioattivo (131 J) attraverso la ghiandola mammaria umana.)
By U. MARINONI and S. AVANZINI. *Ann. Ostet. Ginec.*, **78**, 1075. Oct. 1956. 10 refs.

Study of four lactating women has confirmed that radioactive iodine passes into human milk shortly after administration to the mother, both during lactation and for a short time after its cessation. The iodine content of milk is higher than that of the plasma and also higher than that of saliva or gastric juice. The amount of radioactive iodine passing into the milk is highest during the period of greatest activity of the gland. Higher levels were found in recently lactating mothers than in those in whom lactation had been discontinued for 15 days.

Radioactive iodine should not be given to mothers who are actively suckling, owing to the danger to the foetus. In the cases in this series, the milk was not used to feed the baby. *Josephine Barnes*

118. **Puerperal Surgery and Umbilical Hernia.**

By D. H. BLAKEY. *Lancet*, **2**, 1312–1314. Dec. 28, 1957. 7 refs.

In this paper the author pleads for the greater use of the puerperium as a suitable time for the performance of certain operations, with advantage to both the hospital and the mother. In particular, he suggests that repair of an umbilical hernia should be done in this period so that advantage is taken of the sudden reduction in abdominal contents by delivery. *H. H. Fouracre Barns*

MATERNAL MORTALITY

119. **A Critical Review by the Ministry of Health of England and Wales of the Report of a Thousand Maternal Deaths.**

By A. J. WRIGLEY. *S. Afr. med. J.*, **31**, 1057–1066. Oct. 19, 1957. 4 tables. 10 figs. 4 refs.

The methods employed for obtaining information for this report are described. In 43 per cent of cases there was a primary avoidable factor, and in a further 10 per cent a doubtful factor. Toxaemia, haemorrhage, abortion and pulmonary embolus accounted for two-thirds of the deaths. In 316 deaths associated with pregnancy and childbirth, 121 were due to heart disease. With regard to toxaemia, avoidable factors were present in 52 per cent of cases. The increasing risk of death from toxaemia with increasing age and parity is stressed. The avoidable factor incidence was much lower in women who had placed themselves under hospital supervision.

Two hundred and twenty women died as a result of haemorrhage. There was a greater risk with domiciliary care in patients of higher age and parity. The value of the emergency obstetrical team is stressed. Pulmonary embolism accounted for 138 deaths and abortion for 153. Of the 121 cardiac deaths, one-third died during pregnancy, one-third died during labour or immediately post-partum, and the remainder died in the puerperium. Caesarean section was responsible for 183 deaths. The incidence of Caesarean section in the 3-year period was 28 per 1,000 deliveries, and the mortality was 4 per 1,000. The main causes of death were haemorrhage in 20 per cent, pulmonary embolism in 18·3 per cent, shock or collapse in 17·1 per cent, sepsis 8 per cent, ileus 6·9 per cent and asphyxia from inhaled vomitus in 6·9 per cent. Suggestions are made for the reduction of this incidence. Apart from careful antenatal care, the author stresses that much more attention should be paid to the general health of the patient. *L. J. Abramowitz*

INFANT

120. **Haemolytic Disease of the Newborn. The Fate of 246 Rhesus-Incompatible Pregnancies.**

By G. A. KELSALL, J. R. H. WATSON and G. H. VOS. *Lancet*, **2**, 1255–1258. Dec. 21, 1957. 2 tables. 9 refs.

In a previous article two of the authors concluded that in cases where the Rh-antibody titre of the mother's serum rose considerably in the last five weeks of pregnancy induction of labour gave significantly better results than allowing the pregnancy to proceed to spontaneous delivery. This present paper deals with the fate of the live-born infants who were followed up, when possible, to the age of 18 months. Of the 207 live-born infants there were 186 babies who survived the neonatal period. With the exception of one spastic baby the development of all cases seen was within normal range and there seemed to be no abnormality, intellectual or motor. At 18 months of age there were at least 158 (64 per cent) normal infants resulting from the 246 incompatible pregnancies. The infants in the series considered were delivered either spontaneously or by premature induction of labour. Both groups were treated by exchange transfusion in the same way. The ultimate outcome of the survivors at 18 months showed no difference between the two groups.

H. H. Fouracre Barns

121. **Clinical Experience with Hemolytic Disease of Newborn Infants.**

By T. R. BOGGS. *J. Amer. med. Ass.*, **165**, 1237–1240. Nov. 9, 1957. 4 figs. 3 refs.

Tabulated results are given of 251 infants with haemolytic disease treated at the Hospital of the University of Pennsylvania and the Children's Hospital of Philadelphia. Early diagnosis and management are necessary in the treatment of this disease. In 97 per cent of the full-term infants seen before the age of 12 hours the results were good and death occurred in 3 per cent only because of critical illness at birth. In those referred after the age of 12 hours only 88 per cent made satisfactory progress and failure was largely due to cerebral palsy. In premature infants a successful result was achieved in 76 per cent. Treatment was aimed to maintain the total serum bilirubin level below 20 mg. per 100 ml. during the first five days of life.

One-third of the infants made satisfactory progress without exchange transfusion. One-third required a single exchange transfusion and one-third required multiple exchange transfusions. While early termination of pregnancy may be beneficial in carefully selected cases, the indiscriminate practice of induction of labour or Caesarean section before term though resulting in a greater number of live-born infants leads to a significantly lower over-all success rate because of a much higher neonatal mortality. *D. W. James*

122. **Management of Erythroblastosis Fetalis and ABO Hemolytic Disease.**

By C. B. HYMAN and P. STURGEON. *West. J. Surg. Obstet. Gynec.*, **65**, 384–389. Nov.-Dec. 1957.

This is a good general survey of treatment but no new ideas or techniques are described. *D. C. A. Bevis*

123. **Impending Fetal Death In Utero Due to Isoimmunization: The Maternal Syndrome: Report of Three Cases.**

By R. C. GOODLIN. *Obstet. Gynec.*, **10**, 299–302. Sept. 1957. 4 refs.

In its most complete form the maternal syndrome of impending foetal death from erythroblastosis foetalis consists of marked weight gain, ankle oedema, hydramnios, and generalized pruritus. Once this syndrome makes its appearance, the foetal prognosis is virtually hopeless.

Between 1951 and 1956 there were 27 foetal deaths *in utero* due to isoimmunization at the University of Minnesota Prenatal Clinic. Ten of these exhibited the maternal syndrome of impending foetal death, and details are given about 3 of them. All 10 had significant weight gain, 7 had generalized pruritus, 8 had hydramnios, and 5 had albuminuria. Pruritus distinguishes the condition from toxaemia. As far as can be determined, the foetus was alive at the onset of the syndrome, but, even if removed from the uterus at this stage, failed to survive. *J. G. Dumoulin*

124. **Maternal Age and Foetal Oxygenation.**

By E. P. N. TURNBULL and D. BAIRD. *Brit. med. J.*, **2**, 1021–1024. Nov. 2, 1957. 3 tables. 3 figs. 8 refs.

The aim of this investigation was to determine whether foetal oxygenation diminishes with maternal age. One hundred primigravidae from the Midwifery Department, University of Aberdeen, were studied. In all, pregnancy was clinically normal. Spontaneous delivery occurred in 73 cases, low forceps delivery under pudendal block in 19, and Caesarean section under spinal anaesthesia was performed in 8. Samples of arterial and venous cord blood were withdrawn anaerobically immediately after delivery. The oxygen content was measured by the Van Slyke and Neill method (*J. biol. Chem.*, 1924, **61**, 523) as modified by Orcutt and Waters (*J. biol. Chem.*, 1937, **117**, 509) in the cases where the mother had been given nitrous oxide analgesia.

Results showed that oxygen saturation tended to decrease both with maternal age and gestation time, the effects being statistically significant. The length of labour and weight of the baby had no effect on oxygen levels.

In Aberdeen since 1953, labour has been induced routinely by rupture of the membranes in primigravidae aged 25 or more who are undelivered by the end of the 41st week of gestation. Caesarean section has been resorted to more frequently on signs of foetal distress. Apparently as a result, the number of unexplained foetal deaths in the elderly and postmature patient have been substantially reduced, and are now no higher than the younger age groups. The authors recognize, however, that an accurate method of predicting the oxygen saturation level in any particular foetus is badly needed. *E. Wilson*

125. **Blood Sugar Levels in the Newborn of Diabetic Mothers.** (Über das Blutzuckerverhalten von Neugeborenen diabetischer Mütter.)

By M. WORM. *Geburtsh. u. Frauenheilk.*, **17**, 1110–1114. Dec. 1957. 5 figs. 18 refs.

Working in the Institute for Research and Treatment of Diabetes in Karlsburg, the author has studied the blood-sugar levels of 101 infants born of diabetic mothers, during the first 24 hours of life. Estimations of the blood sugar were made on cord blood and on capillary blood collected 8–12 minutes, 3 hours and 24 hours after birth. At birth the maternal blood sugar was also estimated.

The infants' blood sugar at birth was directly related to the maternal levels. Thereafter it fell rapidly to reach the lowest level 3 hours after birth and then rose again slowly until after 24 hours the blood sugar levels were the same as those in babies born of normal mothers. The administration of glucose orally (2 g., in expressed breast milk at 4-hourly intervals) during the first 24 hours of life had no effect on the blood sugar curves. Lower blood sugar levels were observed in the less mature infants.

Of 148 babies born of diabetic mothers, 21 died within the first 10 days of life. The blood sugar curves of these babies were the same as those obtained from the infants that survived. Of these, 15 died of hyaline membrane, 3 of congenital abnormalities, 2 of birth injuries and the remaining baby died from aspiration of vomit. In no case was there an unexplained death that might have been attributed to hypoglycaemia. *Peter J. Huntingford*

126. **Embryopathy and Perinatal Mortality in Diabetic Pregnancies.** (Embryopathie und perinatale Sterblichkeit bei Früchten diabetischer Mütter.)

By M. WORM. *Zbl. Gynäk.*, **79**, 1853–1857. 1957. 2 tables.

In a study of 163 foetuses of diabetic women, delivered in the course of 4 years, the incidence of malformation was 6·5 per cent. There was no predominance of any particular type of abnormality. Poor control of the diabetes increased the incidence of hydramnios during the later months. Owing to the diabetogenic effect of pregnancy the insulin requirements rise in the diabetic patient. For these reasons the dosage of insulin was raised to the limit of tolerance so that the urine was kept nearly free of glucose, irrespective of the known lowering of the renal threshold in pregnancy. With such management, the author found that intra-uterine death and hydramnios were rare.

The most common cause of neonatal death in these cases is aspiration of liquor and hyaline membrane formation in the lungs. The former is more common amongst children delivered by Caesarean section; the latter occurs particularly in prematures.

In a series of 36 patients on a high insulin dosage in order to keep the blood sugar at about 100 mg. per cent, the majority was delivered per vaginam after the 37th week and 5 children were lost (13·9 per cent).

This compares favourably with a series of 127 women delivered mainly by Caesarean section 4 to 5 weeks before term, in whom the blood sugar varied between 100 and 200 mg. In this group 26 children (20·5 per cent) were lost.

The author concludes that with strict control of the diabetes routine Caesarean section may not be necessary.

Bruce Eton

127. **Frequency of Defects in Infants Whose Mothers had Rubella During Pregnancy.**

By M. GREENBERG, O. PELLITTERI and J. BARTON. *J. Amer. med. Ass.*, **165**, 675–678. Oct. 12, 1957. 7 refs.

From the New York City Department of Health the authors report the results of actual examinations of infants born to mothers in whom rubella during pregnancy was diagnosed by a physician. Of 104 women who had rubella during the first trimester of pregnancy, 27 per cent gave birth to normal infants, 3 per cent to congenitally malformed babies, 3 per cent to stillbirths, and 12 per cent to other nonviable foetuses. Therapeutic abortions were performed on 46 per cent, and 10 per cent of the cases were lost from the study.

The incidence of congenital deformities among the live-born babies of women with rubella during the first trimester of pregnancy was 9·7 per cent. Because of the high therapeutic abortion rate a proper control group was not possible. In New York City notification of congenital malformations is required on the birth certificate, and in a similar study of pregnant women who did not have rubella during pregnancy the incidence of congenital malformation was 7 per cent and the central nervous system and the heart were involved in only 1·9 per cent of these.

Although rubella appears to increase the likelihood of malformation in the central nervous system and heart the high rates of incidence reported previously are exaggerated and therapeutic abortion should not become routine. It is suggested that young children should be encouraged to contract rubella as a preventive measure.

D. W. James

128. **The Choice Between Death from Postmaturity and Death from Induction of Labour.**

By G. F. GIBBERD. *Lancet*, **1**, 64–66. Jan. 11, 1958. 2 tables. 3 refs.

A large series of deliveries is analyzed to obtain the incidence of stillbirth due to anoxia. In pregnancies of 41 weeks or greater duration the incidence of stillbirth due to postmaturity itself was 1·1 per cent. In a series of 68 surgical inductions performed for postmaturity there were 4 stillbirths due to intranatal asphyxia. No figures are available for the results of induction of labour by medical means.

The author draws attention to the fact that with the routine use of a completely harmless method of induction of labour very few infants would be saved from the fate of anoxia due to postmaturity. Whereas from the figures of surgical inductions the danger to foetal life from this procedure is only too apparent.

H. H. Fouracre Barns

GYNAECOLOGY

DISORDERS OF FUNCTION

129. **Long-Acting Estrogens in Amenorrhea and the Menopause.**

By A. I. GURTMAN, J. A. ANDRADA, M. H. G. BLATT, J. A. EPSTEIN and H. S. KUPPERMAN. *Obstet. Gynec.*, **10**, 261–265. Sept. 1957. 11 refs.

The effectiveness of 2 long-acting oestrogenic compounds was evaluated in a group of 83 menopausal and 27 amenorrhoeic patients. The preparations were oestradiol 17-beta-n-valerate and oestradiol 17-cyclopentyl-propionate. They are comparable and equally effective substances which may be administered at intervals of 2 to 3 weeks to achieve an adequate therapeutic response. They offer a convenient mode of administration (intramuscularly) to those patients in whom oral oestrogenic therapy is difficult or undesirable.

J. G. Dumoulin

130. **9 α-Bromo-11-Ketoprogesterone: Another New Orally Effective Substance with Progestational Activity.**

By G. L. WIED and M. E. DAVIS. *Obstet. Gynec.*, **10**, 411–417. Oct. 1957. 2 tables. 5 figs. 11 refs.

Three women whose ovaries had been removed were given 1 mg. diethylstilboestrol daily. On the 16th day of the test cycle the oestrogen therapy was supplemented by daily doses of from 60 mg. to 160 mg. of 9 α-bromo-11-ketoprogesterone. Three cycles were produced in each patient.

The endometrium showed secretory changes each time most marked when the daily dose was 120–160 mg. Vaginal epithelium, cervical mucus and basal body temperature all reacted in a similar way.

The new compound is an effective substance with definite progestational activity when taken by mouth, and seems to be more effective than the generally used anhydrohydroxyprogesterone.

J. G. Dumoulin

131. **Sex Steroid Influence on the Ageing Process.**

By W. H. MASTERS. *Amer. J. Obstet. Gynec.*, **74**, 733–746. Oct. 1957. 67 refs.

The author apparently regards the menopause as a pathological process in which the pituitary-adrenal axis continues to function with production of adrenal corticoids, but the secretion of sex steroids by the ovary fails. This causes, in addition to atrophy of the sex organs, loss of protein and calcium from the long bones and osteoporosis. As replacement therapy he uses testerone which has about one-tenth of the luteal action of progesterone, and oestrogens in a 20 to 1 ratio. This improves memory and mental capacity and restores the genital organs, except the ovary, to normal size and function without causing any endometrial hyperplasia or uterine bleeding. It causes hirsutism or hoarseness in 20 per cent of patients, and if it does so the testosterone oestrogen ratio should be reduced to 15 to 1.

F. J. Browne

132. **The Effects of Oestrogens and Prednisolone on the Genital Apparatus of the Castrated Guinea Pig.** (Sulle possibili interferenze fra estrogeni e prednisolone a livello dell'apparato genitale di cavia castrata.)

By C. Luraschi. *Ann. Ostet. Ginec.*, **78**, 1061. Oct. 1956. 48 refs.

A series of 24 guinea pigs were divided into two groups, after castration; the first group received treatment 30 days after castration and the second group 5 days after castration. Each group was further divided into four; the first group were controls, the second received oestradiol valerianate, the third group received prednisolone and the fourth oestradiol and prednisolone. Histological observations were made on the changes in the vagina and uterus.

It was found that the genital apparatus of castrated guinea pigs responded to doses equivalent to those used in human therapy. Prednisolone induces a characteristic hypertrophy of all the layers of the uterine horns and the vagina. Abundant mucous secretion appears in the lumina of the uterus and vagina. There was no notable difference in the response in animals treated some time after castration from that in those who received treatment a short time after.

Treatment with oestrogen induces the typical follicular reaction, hypertrophy and hyperplasia of the muscle with increase in weight of the organs and hyperplasia of the endometrium and vaginal epithelium.

Administration of oestrogen and prednisolone together gives an intermediate picture and it is concluded that cortical hormones interfere to some extent with the action of oestrogens. Prednisolone has an anti-oestrogenic effect and not a progesterone-like effect.

Josephine Barnes

INFECTIONS OF THE REPRODUCTIVE ORGANS

133. **The Frequency of Colpitis on Account of Trichomonas Vaginalis.** (La frecuencia de las colpitis por trichomonas vaginales.)

By M. L. Perez and O. Blanchard. *Obstet. Ginec. lat.-amer.*, **15**, 183–186. 1957.

A review is presented of the various factors which can be taken into consideration in influencing the existence of vaginitis due to *Trichomonas vaginalis*. The authors state that as many as 40 per cent of all patients attending their clinic are found to have an infestation with this organism in the vagina. The great majority of their cases occurred between 20 and 40 years of age, and cases were rare before 15 and or after 60. Married women gave the greatest incidence, but the writers consider that this was not because the condition was rare among unmarried women, but because single women who exposed themselves to possible infection by coitus commonly used a chemical contraceptive, which had a disinfectant action. In 500 private patients, they record a frequency of 32 per cent, from which they conclude that social status, in places where hospital clinics are free and easily available, is not a significant factor. On the other hand they maintain that there is a seasonal outbreak of the infection in the spring and early summer, which they attribute to a change in food and habits. They also support the theory that the infestation is related to psychomatic conditions, and that some women are carriers without being aware of it. In their experience, 1 per cent of women with the *Trichomonas vaginalis* in the vagina are unaware of its presence because of the absence of symptoms.

John F. Foulkes

134. **Tuberculosis of the Pelvic Organs.**

By L. W. Cox. *N.Z. med. J.*, **56**, 305–313. Aug. 1957. 3 figs. 11 refs.

The author presents a general description of the disease and treatment as it is recognized today. In New Zealand the incidence of all forms of tuberculosis is diminishing as a result of earlier diagnosis, and of more concentrated attack by antibiotics and surgery. Between 1947 and 1956 in Dunedin, only 17 cases of pelvic tuberculosis were discovered. The results of treatment are recorded.

From the Author's Abstract

135. **Cytochemical and Cytomorphological Changes in the Leucocytes in the Peripheral Blood in Female Genital Tuberculosis.** (Aspetti citochimici e citomorfologici dei leucociti del sangue periferico nella tbc. genitale femminile.)

By G. Spondrini, C. Savi and G. Cigada. *Ann. Ostet. Ginec.*, **78**, 1106. Oct. 1956. 94 refs.

Observations have been made on the white blood cells in 21 cases of female genital tuberculosis. Variations in the cytology and cytochemistry of the leucocytes have been observed and these changes are to some extent related to the severity of the disease; the changes comprise an increase of neutrophils and of Mommsen positive lymphocytes. In the neutrophils, glycogen is increased and the lipid content decreased.

Clinical improvement in the disease leads to a return to the normal leucocyte pattern. Similar changes have been observed in patients suffering from pulmonary tuberculosis.

Josephine Barnes

NEW GROWTHS OF THE REPRODUCTIVE ORGANS

136. **Diabetes and Altered Carbohydrate Metabolism in Patients with Cancer.**

By A. S. Glicksman and R. W. Rawson. *Cancer*, **9**, 1127–1134. Nov.-Dec. 1956. 8 tables. 5 figs. 46 refs.

Nine hundred and fifty patients were studied. The incidence of diabetes in cancer patients was 36·7 per cent and in patients without cancer it was 9·3 per cent. The highest incidence by site of cancer was the pancreas (80 per cent), the next highest the endometrium (64 per cent) and the lowest the uterine cervix (16 per cent). The authors conclude that further studies on these lines may yield insight into the basic problem of cancer.

S. Way

137. **Pruritus, Kraurosis Vulvae and Carcinoma of the Vulva.** (Pruritus, Kraurosis vulvae und Vulvakarzinom.)
By H. Böttger and E. Dittmann. *Geburtsh. u. Frauenheilk.*, **17**, 1097–1109. Dec. 1957. 4 tables. 4 figs. 65 refs.

The authors have reviewed the literature concerning the nature, the histology and the aetiology of pruritus and kraurosis vulvae. They have followed up 160 cases treated at the gynaecological clinic of the University of Kiel, from 1948–1956. There were 82 cases of pruritus and 78 cases of kraurosis. None of the patients with pruritus and 7 of those with kraurosis subsequently developed carcinoma of the vulva. The incidence of carcinoma on kraurosis (9 per cent) is about the same as the incidence of carcinoma in other sites where there is a focus of chronic irritation, e.g., in gastric ulcer.

[The authors have not defined at all clearly the way in which they have classified their cases. It would seem that some cases of leukoplakia are included in the pruritic group, but on the other hand their histological description of the changes found in kraurosis would also be suitable for leukoplakia.]

Peter J. Huntingford

138. **Follicular Hormone and Carcinoma of the Corpus Uteri.** (Follikelhormon und Korpuskarzinom des Uterus.)
By H. Behrens. *Geburtsh. u. Frauenheilk.*, **17**, 1126–1135. Dec. 1957. 8 figs. 40 refs.

The author has reviewed 6,059 cases of glandular hyperplasia and 1,066 cases of adenocarcinoma of the endometrium treated in the gynaecological clinic of the University of Leipzig, from 1937–1956.

Seventy per cent of the carcinomata occurred 3 years or more after the menopause. The peak of incidence of glandular hyperplasia occurred 10 years earlier than in patients with carcinoma of the body of the uterus, at 45 years of age.

In 29 cases both glandular hyperplasia and adenocarcinoma were present in the endometrium. As the age distribution curves for the 2 conditions overlap, this coincidence of the diseases was no more than might have been expected from chance.

In the 43 cases of carcinoma diagnosed during menstrual life, any unaffected endometrium that was present was in the proliferative or secretory phase of the cycle. In the remaining patients with carcinoma of the body of the uterus, all of whom were post-menopausal, any endometrium which was found was atrophic. There was never any evidence of an oestrogenic influence on the endometrium.

The author studied the vaginal epithelium of 60 cases of carcinoma of the corpus uteri, in women 3 years after the menopause and in 60 control cases. He found no evidence of increased oestrogenic activity in the patients with carcinoma.

In the Leipzig clinic there have been 43 granulosa or theca cell tumours in the last 20 years. Two of these were associated with carcinoma of the corpus uteri and 2 further cases showed atypical hyperplasia, suggestive of malignancy.

The author has followed 135 cases of atypical endometrial hyperplasia and 8 of these developed carcinoma of the uterus.

The author concludes that the follicular hormones do not play an essential part in the development of carcinoma of the body of the uterus.

Peter J. Huntingford

139. **The Vascular Pattern in the Incipient Carcinoma.** (Über das Gefässbild beim beginnenden Karzinom.)
By E. H. Krüger. *Zbl. Gynäk.*, **79**, 1669–1677. 1957. 16 figs. 25 refs.

This is a report from the Gynaecological Department of the University of Halle on a study of the appearances of the small vessels seen on colposcopic examination of the cervix in the early stages of carcinoma. The minute vessels on the surface of a carcinoma frequently have corkscrew and hairpin shapes and always show variations in calibre. Congested vessels have a bizarre appearance and may run for long stretches without giving off branches. They form a network, but arborization, as is seen in the normal transition zone ("Umwandlungszone") does not occur. The vessels can be seen with the ordinary colposcope, but can be rendered clearer by the use of a green filter and ultra-violet light.

Apart from subtle shades of colour and differences in thickness, the degree of atypical patterns on the portio is an important colposcopic means of detection of early carcinoma.

Bruce Eton

140. **Long-Range Studies of the Biologic Behavior of the Human Uterine Cervix. II. Histology, Cytology, and Clinical Course of Cervical Disease.**
By R. R. De Alvarez, D. C. Figge and D. V. Brown. *Amer. J. Obstet. Gynec.*, **74**, 769–791. Oct. 1957. 6 tables. 5 figs. 27 refs.

This is a beautifully planned prospective study of 954 healthy women whose average age was 42 years but ranging from 14 years to 83. The women were examined at 6-monthly intervals and each examination involved a clinical history and examination, a vaginal smear from the posterior fornix and another from the cervical canal, and a punch biopsy at the squamo-columnar junction. All biopsy material was examined by a single pathologist, and all smears by one cytologist. When cancer was suspected the patient was admitted to hospital for further examination, usually by sharp conization. Such a study would, it is believed, eliminate the influence of selective factors and make available sequential histological and cytological material collected during the incipient stages of disease, particularly malignant disease.

The report contains the results of 5 consecutive examinations extending over 2½ years and obviously the research needs to be extended for a much longer period, perhaps 10 years or more when the conclusions might be most valuable. At the present time the principal results of the investigation can be briefly summarized as follows: squamous metaplasia of surface or glandular epithelium was present in 25 per cent of all biopsies, but there was no

evidence that it tended to become malignant. Fifteen per cent of patients with suspicious smears showed atypical basal cell hyperplasia on biopsy. The vaginal plus cervical smear, or a single cervical biopsy, seemed to be of equal value in diagnostic screening for cervical cancer but in each method there was 20 per cent of false negatives. Among the patients known to have cancer of the cervix the single cervical biopsy failed to reveal its presence in 14·3 per cent. The incidence of development of cancer of the cervix in the group of women during the time they were under observation was 0·5 per cent per year. *F. J. Browne*

141. **The Use of the Colposcope in Gynaecological Practice.** (Utilidad de la colposcopia en la práctica ginecólogica.)

By R. M. Gori and J. D. Elias Costa. *Obstet. Ginec. lat.-amer.*, **15**, 166–167. 1957.

It is claimed that the colposcope is of immense value in gynaecology, and the authors express surprise that it is not universally used. Every patient attending their clinic is examined with this instrument. Only 42 per cent of women are found to have a healthy cervix, and as many as 47 per cent show evidence of islets of glandular tissue resulting from earlier erosion. Their main reason for developing the practice of colposcopy was not with the intention of diagnosing carcinoma directly, but rather to be able to localize areas adjacent to inflammatory lesions where a biopsy would be most likely to find early neoplastic change.

To justify their routine use of this instrument the writers quote the findings of Limburg, who reported that during the years 1945–48, without the use of the colposcope, out of every 100 cases of carcinoma of the cervix diagnosed in his clinic 4·4 were grade 0 and 18·4 grade 1. During the next five years, however, when every cervix was systematically inspected with the colposcope, he found that out of every 100 cases of carcinoma of the cervix 30 were grade 0 and 34·7 grade 1.

John F. Foulkes

142. **Influence of Prophylactic Routine Colposcopy on the Stage Distribution of Carcinoma of the Cervix.** (Der Einfluss systematischer kolposkopischer Vorsorgeuntersuchungen auf die Stadienverteilung des Kollumkarzinom.)

By R. Hohlbein. *Zbl. Gynäk.*, **79**, 1684–1695. 1957. 4 tables. 5 figs. 37 refs.

It is generally accepted that in the present state of knowledge the chances of improving the prognosis of carcinoma of the cervix depend mainly on early diagnosis. Apart from cytology, colposcopy has in recent years increasingly proved its value in this respect. With this in mind, a large-scale colposcopic service was provided in the Dresden area (under the directorship of Professor R. Ganse). In addition to special out-patients' sessions, colposcopic mass examinations were carried out in factories by trained medical specialists. The service was highly organized and included public lectures. As a result, 95,427 examinations were carried out between 1947 and 1956. This led to the detection of 279 cases of highly atypical epithelium (0·29 per cent); 283 of carcinoma of the cervix (0·3 per cent); and 108 other carcinomas (0·11 per cent). Most of these cases of early carcinoma or pre-carcinoma were admitted to the Dresden Centre, A study of the clinical material showed that with the expansion of the service the incidence of early stages increased, with a relative decrease of Stages III and IV. Thus, Stage I cancers rose from 16·4 per cent in 1950 to 43·5 per cent of all Stages seen in 1954. Correspondingly, Stages III and IV decreased from 66·7 per cent to 24·7 per cent in 1954. Stage 0 cases rose from 2·7 per cent in 1949 to 32·8 per cent in 1953.

The author discusses possible objections to mass colposcopy. Cancerophobia is less likely to be fostered by instruction of the public through qualified medical personnel than by the superficial reporting of the illustrated lay press.

Any patient with positive findings is, in the first instance, referred back to her own general practitioner who thus does not lose the patient, although he will probably send her to the nearest centre for treatment.

The question as to whether or not such a service is uneconomical is answered by the following considerations: the cure rate for Stage 0 carcinoma is about 95 per cent, that for Stage I, 75 per cent; any case found to be in these two stages almost certainly means a life saved.

Bruce Eton

143. **Follow-Up on Cervical Epithelial Abnormalities.**

By B. Peckham and R. R. Greene. *Amer. J. Obstet. Gynec.*, **74**, 804–815. Oct. 1957. 8 tables. 4 figs. 7 refs.

This is a retrospective study of specimens, mostly biopsies, from 489 women, 69 of whom were pregnant, undertaken to clarify the significance of abnormalities of cervical epithelium preceding the development of cancer *in situ*. The follow-up varied from 12 to 97 months, 11 of the cases being followed for 48 months or more.

In 50 per cent of the 133 patients in whom the original cervical biopsy showed atypical basal cell hyperplasia later biopsies showed that the lesion had disappeared; in 35 per cent there was no change; in 9 per cent it had progressed to an "equivocal" lesion (by which is meant that the abnormalities of the epithelium extended through the whole thickness of the epithelial covering but were inadequate to justify diagnosis of cancer *in situ*); 8 cases (6 per cent) had progressed to pre-invasive cancer.

The results demonstrate the need to follow up all cases of atypical basal cell hyperplasia and those in which the lesion is equivocal. There was no significant difference between the disappearance rate of epithelial abnormalities of the cervix discovered in the 69 pregnant women and in those who were not pregnant which is contrary to the usual teaching that 94 per cent of them have returned to normal by 6 months after delivery.

In atypical basal cell hyperplasia the vaginal smear may be normal. Thus in 21 per cent of Peckham and Greene's cases the smear was negative but biopsy showed either atypical B.C.H. or an equivocal lesion. The frequency of regression of both these was in inverse proportion to the severity of the lesion. *F. J. Browne*

144. **Clinical Observations in Cases of Intra-Epithelial Carcinoma.** (Zur Klinik des Oberflächenkarzinom.)

By G. F. WINTER. *Zbl. Gynäk.*, **79**, 1889–1900. 1957. 1 table. 3 figs. 11 refs.

The author collected a comprehensive series of 3,764 invasive and 254 intra-epithelial (Stage 0) carcinomas of the cervix from the gynaecological clinics of 8 universities and of 8 other hospitals. The object was to investigate the relationship between the two cancers which would have a bearing on the decision regarding the appropriate treatment for Stage 0 carcinoma.

Regarding the question of the incidence of the intra-epithelial form of cervical cancer, he found that there was considerable variation. In 15 centres the incidence of the intra-epithelial form of cervical cancer varied from 0 per cent to 32 per cent, with a statistical mean of 6·7 per cent. The sixteenth centre was a specialized cancer detection unit where the incidence amounted to 75 per cent. In many centres the incidence has risen in recent years with the increasing use of cytology and colposcopy. It would seem that the wider the search the more cases are detected.

The second question put by the author is: how often did a cervical biopsy reveal Stage 0 cancer? Apart from cases of invasive carcinoma, he observed 53 cases of Stage 0 cancers amongst 534 biopsy specimens. With the increasing use of the Ayre type of ring biopsy the percentage of Stage 0 cancers at his own centre rose from 5 per cent in 1954, to 10 per cent in 1955 and 20 per cent in 1956.

The third problem was to find out how often the diagnosis of Stage 0 cancer based on a biopsy had to be changed to one of invasive cancer when the whole portio was examined (about 100 sections spaced at regular intervals). Thus, of the 53 cases of Stage 0 cancer, 10 showed subsequently undoubtedly invasive and 3 possibly invasive carcinoma. This observation leads to obvious therapeutic conclusions. It also affirms the superior value of the circular biopsy over other types. The method of selecting a suitable area for a localized biopsy by means of colposcopy is not infallible, as it occasionally fails to reveal the site of an intra-epithelial or invasive carcinoma.

Bruce Eton

145. **Therapy of Carcinoma In Situ: Implications from a Study of its Life History.**

By R. W. TE LINDE, G. A. GALVIN and H. W. JONES, JR. *Amer. J. Obstet. Gynec.*, **74**, 792–803. Oct. 1957. 2 tables. 4 refs.

After a retrospective review of patients with invasive cancer of the cervix or cancer *in situ*, and a study of cases of cancer *in situ* that were not treated, the authors concluded that in most cases invasive cervical cancer is preceded by cancer *in situ* and cancer *in situ* by basal cell hyperplasia (B.C.H.), but that all cases of B.C.H. do not progress to cancer *in situ*, or all cases of cancer *in situ* to invasive cancer. This, however, may be due to the follow-up being too short, or to patients dying of other causes before the more serious lesion developed.

Review of biopsy material that had been removed from the cervix 1 to 20 years before invasive cancer was found showed that in 2 cases, one in Stage II and another in Stage I, the cervix was normal 5 years previously. In another case cancer *in situ* was shown to have been present 20 years before a Stage II invasive cancer was diagnosed, and in another one year before diagnosis of a Stage II invasive cancer. On the other hand B.C.H. was found to have been present for 6 years and cancer *in situ* for 7 years without cancer having developed.

Because of experience in 6 cases of cancer *in situ* in which hysterectomy was not done and which later developed invasive cancer, the authors conclude that the unequivocal diagnosis of cancer *in situ* is an indication for prompt hysterectomy with removal of a generous vaginal cuff. In B.C.H. because of the small percentage of cases which progress to more serious lesions a very conservative attitude is advised with careful follow-up. A difficult problem arises when cancer *in situ* is found in a young woman who has never had a child. Here their plan has been to tell the patient the facts "in a completely unbiased manner". So far all have chosen immediate hysterectomy. If one should choose to undergo a pregnancy it should be allowed only under the closest personal observation.

In the discussion following this paper D. G. Morton stated that it is not permissible to make a diagnosis of cancer *in situ* unless one has studied thoroughly all of the tissue contained in a sizeable cone removed from the cervix to exclude invasive cancer. This meant a cone with a base of 2 cm. and its apex at the internal os. This can only be obtained in hospital under anaesthesia. He believed that when cancer *in situ* had been diagnosed in this way conservatism was justified in the case of a young woman who desires a child and is willing to co-operate about follow-up study.

F. J. Browne

146. **Carcinoma of the Cervix at Chelsea Hospital for Women, 1933–56.**

By J. B. BLAIKLEY, M. LEDERMAN and C. A. SIMMONS. *Lancet*, **2**, 1329–1337. Dec. 28, 1957. 17 tables. 1 fig. 4 refs.

The authors record the results of cases treated by surgery, radiotherapy and a combination of both methods over the years. Since 1944 the patients have been treated at a Joint Clinic conducted by a surgeon and radiotherapist. The results are considered on the basis of the 5-year cure rate. Since the formation of the Joint Clinic the results of treatment have greatly improved. The 5-year survival-rate for patients treated by Wertheim's hysterectomy (Stages I, II and III) rose from 40·8 per cent to 53·5 per cent and those by radiotherapy (Stages I and II) from 26·4 per cent to 51·2 per cent. The 5-year survival-rate for Stage I cases treated by Wertheim's hysterectomy since 1944 was 65·1 per cent and that by radiotherapy was 60·4 per cent. By excluding 13 of the 48 Stage I patients treated by radiotherapy alone because some part of their radiation treatment had already been given before presentation at the Joint Clinic, the 5-year survival-rate became 69 per cent. By further excluding all

cases where death took place from intercurrent disease the 5-year survival-rate was 77 per cent compared with 67 per cent for Wertheim's hysterectomy. On this evidence the authors conclude that it seems that radiotherapy is not only undoubtedly the correct treatment in inoperable cases but also usually the preferable treatment for operable cases.

[These figures which do not differ significantly by statistical standards show that the 5-year cure rate for Stage I carcinoma of cervix is about the same for radiotherapy as for radical surgery. What is now wanted is information on subsequent progress, i.e., 10-year cure rate analysis.] *H. H. Fouracre Barns*

147. **Lymphatic Channels of Spread of Cervical Carcinoma.** (Le vie di diffusione linfatica nei carcinomi del collo dell'utero.)

By S. PAPADIA. *Minerva ginec., Torino*, **9**, 679–686. Aug. 31, 1957. 3 tables. 1 fig. 69 refs.

This study was made from 135 laparotomies at Bari. The lymph nodes were in six main groups: para-cervical, parametrial, obturator, hypogastric, external iliac and common iliac. The pathways are essentially two: (1) from the para-cervical and parametrial nodes to external iliac and obturator and thence to the common iliac nodes, and even, though rarely, to the peri-aortic and inguinal groups, and (2) from the same para-cervical and parametrial nodes to the hypogastric and common iliac groups. These two pathways may be followed separately or concurrently on one or both sides, the first pathway being the more usual. The incidence of lymphatic involvement was 30·1 per cent over the series, and naturally higher in the more advanced stages of the disease. *W. C. Spackman*

148. **Basal Cells in Vaginal Smears of Patients with Carcinoma of the Cervix.**

By W. LIU. *Cancer*, **10**, 522–528. May-June 1957. 7 tables. 11 figs. 2 refs.

Observations were made on 334 cases at Vincent Memorial Hospital, and 316 cases in the Newcastle Cancer Organization Gynaecological Clinic at Queen Elizabeth Hospital, Gateshead. Three hundred and sixteen non-malignant controls came from the cytological laboratory at the Queen Elizabeth Hospital.

It was found that in every decade of age there was a significant increase in the exfoliation of basal cells in cancer cases and often of cornified cells as well. These increases were at the expense of the pre-cornified cells. *S. Way*

149. **Studies on the Use of Viruses in the Treatment of Carcinoma of the Cervix.**

By R. R. SMITH, R. J. HUEBNER, W. P. ROWE, W. E. SCHATTEN and L. B. THOMAS. *Cancer*, **9**, 1211–1218. Nov.-Dec. 1956. 2 tables. 19 refs.

Some patients with very advanced cancer were treated by direct injection into the tumour of tissue culture suspension of APC viruses. Necrosis of tumour tissue occurred and it is concluded that this was a specific viral effect. Patients with serum antibodies against the viruses showed less response. Despite the extensive tumour destruction produced regrowth occurred in all cases. *S. Way*

150. **Treatment of Carcinoma of the Cervix Recurrent After Surgery.**

By W. W. DANIEL and A. BRUNSCHWIG. *Cancer*, **9**, 1208–1210. Nov.-Dec. 1956. 5 tables.

Recurrence of carcinoma of the cervix after surgery does not necessarily imply a hopeless situation. Surgical excision offers the best hope of cure, but radiation therapy is the only treatment that can be tried for recurrences on the pelvic wall. *S. Way*

151. **Treatment of Recurrent Carcinoma of the Cervix With Cobalt 60.**

By J. F. NOLAN, J. A. VIDAL and J. H. ANSON. *West. J. Surg. Obstet. Gynec.*, **65**, 358–366. Nov.-Dec. 1957. 4 charts. 11 refs.

The Los Angeles Tumor Institute reports the results obtained with a 1,000-curie Cobalt 60 teletherapy unit which has been used since 1952. Eighty-nine patients are considered, 61 of which are post-radiation failures. Only 12 patients are now alive and well, 12 are alive but show evidence of carcinoma and 65 have died of the disease. Radiation dosage has been variable but the effective dose seems to be in the region of 5,300 r. in 42 days; 34 patients were treated with higher dosage, 8 being successful; 39 patients treated with smaller dosage were all failures. Radiation ill-effects were found most commonly in patients with the higher dosage. The impression gained from the work is that if these patients are to be treated by radiotherapy the best results are likely to be obtained from protracted megavoltage techniques.

[Much technical information is given in the original and the discussion is most helpful.] *D. C. A. Bevis*

152. **Evaluation of the Combined Effects of Hematoporphyrin and Radiation. I. Treatment of Carcinoma of the Cervix.**

By H. P. MACK, W. K. DIEHL, G. C. PECK and F. H. J. FIGGE. *Cancer*, **10**, 529–539. May-June 1957. 6 tables. 5 figs. 30 refs.

Twenty-five patients were treated with radiation combined with intravenous haematoporphyrin therapy.

Results were based on "clinical regression of the tumour" plotted against time. Longevity was not appreciably altered although initial response was much better in those treated with haematoporphyrin.

[I and my colleagues have repeatedly pointed out that initial clinical response to irradiation is a poor yardstick to prognosis. This paper seems to confirm that.] *S. Way*

153. **The Treatment of Ovarian Carcinoma in the Gynaecological Department of the University of Würzburg between 1939 and 1952.** (Die Therapie des Ovarial-Karzinom an der Universitäts-Frauenklinik Würzburg von 1939 bis 1952.)

By A. RUMMEL. *Zbl. Gynäk.*, **79**, 1865–1867. 1957.

Two hundred and sixty-four cases of ovarian carcinoma

were classified into 4 groups. Their respective survival rates were: (1) complete surgical removal, 60 per cent; (2) incomplete removal, 10 per cent; (3) inoperable carcinoma found at laparotomy, 0 per cent. The fourth group represents the remainder in whom carcinoma was not proved surgically or histologically. The absolute cure rate was 26·9 per cent.

The therapeutic principles are that every case should be operated if feasible; surgery should be as radical as possible. If an incomplete operation leaves growth in the neighbourhood of the uterus, this organ should be preserved as a radium container. In all other cases it is removed. Post-operative deep X-ray therapy was administered as a routine. Not infrequently a tumour was found to be inoperable at laparotomy, but became operable after deep X-ray therapy.

Bruce Eton

154. **Endometrial Hyperplasia, Endometrial Carcinoma and Endometriosis Produced Experimentally by Estrogen.**

By W. A. MEISSNER, S. C. SOMMERS and G. SHERMAN. *Cancer*, **10**, 500–509. May-June 1957. 2 tables. 11 figs. 18 refs.

The authors had a two-fold objective in this experiment, namely to produce in rabbits endometrial hyperplasia by prolonged and excessive oestrogen stimulation and also to study the relationship of the alloxan-diabetic state to the oestrogen stimulation.

Two cancers arose in 7 rabbits given stilboestrol and 4 in 11 given alloxan and stilboestrol. Alloxan alone, although successful in producing diabetes, gave no cancers and no cancers were seen in the controls. The average time taken for cancer to develop was 418 days.

The authors draw attention to the fact that alloxan diabetes is not the same as diabetes mellitus and believe that a cortisone induced diabetes would have more nearly approached diabetes seen in the human.

S. Way

155. **Endocrine Abnormalities Accompanying Human Endometrial Carcinoma.**

By S. C. SOMMERS and W. A. MEISSNER. *Cancer*, **10**, 516–521. May-June 1957. 2 tables. 4 figs. 25 refs.

Thirty-eight women dying of endometrial cancer were studied at autopsy, and hyperplasias of ovarian cortical stroma and adrenal cortex occurred much more frequently than in non-cancer controls. The pituitary, when available, showed marked differences also as compared with the non-cancer patients.

Changes found in the endocrine glands and target organs with endometrial cancer support a hypothesis of primary pituitary and ovarian hyperfunction.

S. Way

156. **Irradiation Castration.**

By R. W. STANDER. *Obstet. Gynec.*, **10**, 223–229. Sept. 1957. 9 refs.

This report is concerned with the long-term effect of irradiation on the pelvic structures, primarily the endometrium. At the University of Michigan Hospital between 1932 and 1946, 964 patients received external radiation or intra-uterine radium for benign pelvic disorders: 735 of these were followed up and a further 96 cases were known to have died, none of gynæcological cancer.

The 735 patients observed for 10 years or more developed 19 pelvic cancers (2·6 per cent)—14 corpus, 4 ovarian, and 1 vulval. There were no cervical cancers. It seemed that the endometrial cancer incidence was over 3 times greater than expected, a fact that other authors have previously pointed out. This increased incidence seemed to be related to factors involved in the abnormal uterine bleeding for which the patients were irradiated rather than to irradiation *per se*. Thus certain endocrine and constitutional abnormalities such as obesity, diabetes, hypertension and nulliparity were more frequent in those that developed cancer later.

The original slides of the endometrium of the patients who later developed cancer were studied. They showed no specific characteristics to allow prediction that cancer would develop.

J. G. Dumoulin

OPERATIONS

157. **Surgical Treatment of Atresia and Aplasia of the Vagina.** (Chirurgische Behandlung bei Atresien und Aplasien der Vagina.)

By E. YENEN. *Zbl. Gynäk.*, **79**, 1641–1647. 1957. 7 figs. 17 refs.

The author reviews a series of 49 cases of atresia or aplasia of the vagina collected in the course of twelve years. Nine of these followed spontaneous deliveries with dystocia. Healing of the birth injuries resulted in various forms of atresia. Four occurred after forceps delivery. Fourteen cases of acquired partial atresia were non-obstetric, following other trauma or inflammatory processes. In addition, there were 4 cases of haematocolpos and 18 cases of complete aplasia. All patients in the last group were "unequivocally" females. [Chromosomic and hormonal investigations are not mentioned.] In 3 patients, treated surgically, the artificial vagina was lined with amnion. One of these died after 24 hours. In the second the vagina became obliterated again within a short time. In the third case a dilator was fitted into the tunnel, apparently with a better result.

The author successfully carried out a new abdomino-perineal procedure in one case; the two layers of the broad ligament were separated and pulled down to form a lining for the artificial vagina which was then closed at its upper end.

Bruce Eton

158. **The Psychological Impact of Cancer and Cancer Surgery. VI. Adaptation to Hysterectomy.**

By M. G. DRELLICH, I. BIEBER and A. M. SUTHERLAND. *Cancer*, **9**, 1120–1126. Nov.-Dec. 1956. 6 refs.

This is the sixth paper from the Department of Psychiatry at Memorial Hospital, New York, dealing with the psychological adaptation to various types of surgery necessary in the treatment of cancer and benign tumours. In this paper 23 pre-menopausal women who were to undergo operation were examined, 14 had

fibroids and 9 uterine carcinoma. They were studied pre- and post-operatively.

Six patients had delayed seeking treatment for lengthy periods of time and in all fear was the cause of delay. One was afraid she would never work again, another could not trust her husband whilst she was in hospital, and a third thought that examination would reveal serious disease. Even when there was no delay fear was still present in every patient.

First was the fear of surgery. "Everybody hates the knife. People are mutilated and have agony afterwards." The fear of anaesthesia was slight. The fear of cancer caused near panic even in some patients with benign disease. "The doctor recommended operation when they found the fibroid and I wanted the operation in case it turned to cancer. Now I'm afraid to go through with it for fear they will find cancer after all."

The greatest apprehension, however, concerned the loss of the uterus. There was regret over the loss of child-bearing ability, even though in some cases the operation removed the necessity of distasteful contraception. A 35-year old woman stoically accepted advice for hysterectomy but expressed great relief on being eventually told she would have a myomectomy. Loss of menstrual function even when this had been disabling, was not received well by these patients. Some believed it was necessary for the relief of waste products, whilst another thought that its rhythm organized the pattern of her daily life.

Anxiety concerning the loss of sexual activity was very great and some feared the possible destruction of marriage. Many thought "they would never be the same again".

Post-operatively many imaginary symptoms were noted, one patient stating "this operation is bound to weaken you. You are supposed to have all your organs. If you lose one you're not as good as before." Another said "I'm still afraid of my inside. I don't know what to expect but I fear the worst."

The authors conclude by emphasizing the need to allow the patients to discuss their fears with the physician.

[This is an important paper for all gynaecologists and shows that fear of cancer is not the greatest one in the problem of hysterectomy. It is well presented and free from windy psychiatric verbiage. Most of the problems revealed by this study show that ignorance of physiology on the part of the population, and modern folk lore in the form of ignorant neighbourly gossip, are at the bottom of practically all these troubles. Surely the aloofness often shown by the medical profession to lay education cannot escape responsibility for this state of affairs.]

S. Way

159. **Intra-Operational Siting of Tubal Obstruction.** (Localizacion intraoperatoria de la obstrucción tubaria.)

By E. G. MURRAY and A. FOIX. *Obstet. Ginec. lat.-amer.*, **15**, 79–84. 1957. 6 figs. 12 refs.

One of the hazards of plastic surgery for tubal obstruction is stated by the writers to be the uncertainty of not knowing how much of the Fallopian tube is organically obstructed. The authors describe in detail the various techniques for diagnosing obstruction of the tubes, including the more unusual methods such as intra-uterine injections of methylene blue followed by examination with the culdoscope, and salpingography with lipiodol and dyes, etc., during operations, before presenting their own method. This consists of placing a clamp, after opening the abdomen, over the cervix from above so as to occlude it completely. An assistant pinches the opposite tube between his fingers, and air is then introduced into the uterine cavity. Retrograde air insufflation is performed at the abdominal ostium of the tube, whilst the operator likewise endeavours to introduce air from a syringe into the intermediate portion of the tube which does not expand when the proximal and distal parts inflate. By this technique the authors claim to demonstrate whether the tube is solidly blocked for a given length, or only has two strictures with patency between. They claim that with this foreknowledge the surgeon is in a better position to know what approach to make for his plastic procedure. Using this technique for 124 of their cases, the writers state that their only complication has been subserous emphysema.

John F. Foulkes

UROLOGY

160. **Sphincter Incontinence of Urine in the Female. A New Approach to its Classification, Diagnosis and Treatment.**

By A. F. YOUSSEF. *Acta obstet. gynec. scand.*, **36**, 439–459. 1957. 6 figs. 27 refs.

Writing from the department of obstetrics and gynaecology of Kasr-el-Aini Hospital, Cairo University, the author suggests that the designation "sphincter incontinence of urine" should replace the terms stress-incontinence, orthostatic incontinence and functional incontinence, used respectively by English speaking, French and German gynaecologists, because "no increase in the intra-vesical pressure can cause stress-incontinence if the sphincteric mechanism is intact, although if the latter mechanism is deficient a high intra-vesical pressure does increase the severity of the incontinence."

The following classification of sphincter incontinence (s.i.) is suggested:

A. Simple s.i. due to
   (*i*) weakness of the involuntary sphincter mechanism,
   (*ii*) weakness of the involuntary sphincter mechanism plus weakness of the extrinsic or intrinsic voluntary sphincters or both,
   (*iii*) adhesions.

B. S.I. associated with high intra-vesical pressure which may be due to
   (*i*) bladder lesions,
   (*ii*) pelvic tumours,
   (*iii*) faulty innervation.

C. S.I. associated with prolapse.

Twenty-five normal cases, 20 cases of prolapse without s.i., 12 cases of s.i. without prolapse, and 17 cases of s.i. with prolapse were investigated by means of cystometry, cysto-urethroscopy, and sphincterometry; radiological sphincterometrography was also employed.

The clinical significance of sphincterometry is summarized as follows:

(*i*) A sphincter opening pressure during relaxation of less than 40 mm. of mercury confirms the diagnosis of s.i. Such a diagnosis should not be made if this pressure is higher than 80 mm. of mercury.

(*ii*) The efficiency of the voluntary sphincter system can be estimated by subtracting the opening pressure during relaxation from that during contraction.

(*iii*) If the opening pressure during contraction is less than that during relaxation it can be assumed that the presence of adhesions is an important factor in the aetiology of the incontinence.

The author advises individualization of treatment based on pre-operative investigations as outlined above. He recommends Kelly's operation of sphincter plication for mild cases of weakness of the involuntary sphincter alone, Aldridge's sling operation for severe cases of this type, especially those due to congenital hypoplasia or aplasia of the sphincter or to a lower motor neurone lesion, and also in cases of severe s.i. following the successful repair of a vesico-vaginal fistula in the region of the bladder neck. Ingelman-Sundberg's pubococcygeus repair is recommended for cases in which the voluntary sphincter mechanism is also deficient, and vesico-urethrolysis (by the abdominal route, Ingelman-Sundberg, Mulvany, or vaginally, Kennedy) in cases of peri-urethral adhesions, etc.

N. Alders

161. **Disorders of the Urinary Tract Following Irradiation for Carcinoma of the Uterus.** (Über die durch Strahlenbehandlung des Uterus-karzinoms hervorgerufenen Funktionsstörungen der ableitenden Harnwege.)

By H. Muth. *Geburtsh. u. Frauenheilk.*, **17**, 983–995. Nov. 1957. 3 tables. 4 figs. 42 refs.

In order to assess the amount of damage to the urinary tract caused by irradiation treatment of carcinoma of the uterus the author has carried out urological studies in 200 patients in whom there was no evidence of residual disease. The cases were obtained from the gynaecological clinics of the city of Dortmund and the University of Münster, during the years 1951–1956. The 200 cases included 168 cases of stage I and stage II carcinoma of the cervix and 32 cases of carcinoma corpus uteri treated by post-operative irradiation.

There were 22 cases (11 per cent) of unilateral or bilateral ureteric obstruction. In 3 of these cases there was a non-functioning kidney. The author believes that the ureteric obstruction is caused by post-irradiation fibrosis and it occurred 3–12 months after completion of treatment. In only 2 cases were there any symptoms or abnormal physical signs or any evidence of ascending infection.

After intravaginal irradiation the incidence of ureteric damage was 18 per cent as opposed to 4·8 per cent in cases treated by external irradiation only. The incidence of hydronephrosis in cases of carcinoma of the body of the uterus treated by post-operative radiotherapy was 3·1 per cent.

Irradiation therapy of stage I carcinoma of the cervix was complicated by renal damage in 3·2 per cent of cases, this figure rose to 15 per cent in stage II carcinoma of the cervix.

The author quotes the total number of cases of carcinoma of the uterus treated during the period covered by the investigations and he discusses the renal complications resulting from all forms of treatment and due to the disease itself. He also gives the details of the irradiation techniques used.

The author emphasizes that the prognosis is good in cases of hydronephrosis caused by irradiation fibrosis. He considers that the patients should be treated conservatively. If infection occurs and does not readily respond to treatment, re-implantation of the ureter into the bladder should be considered, rather than resorting immediately to nephrectomy.

Peter J. Huntingford

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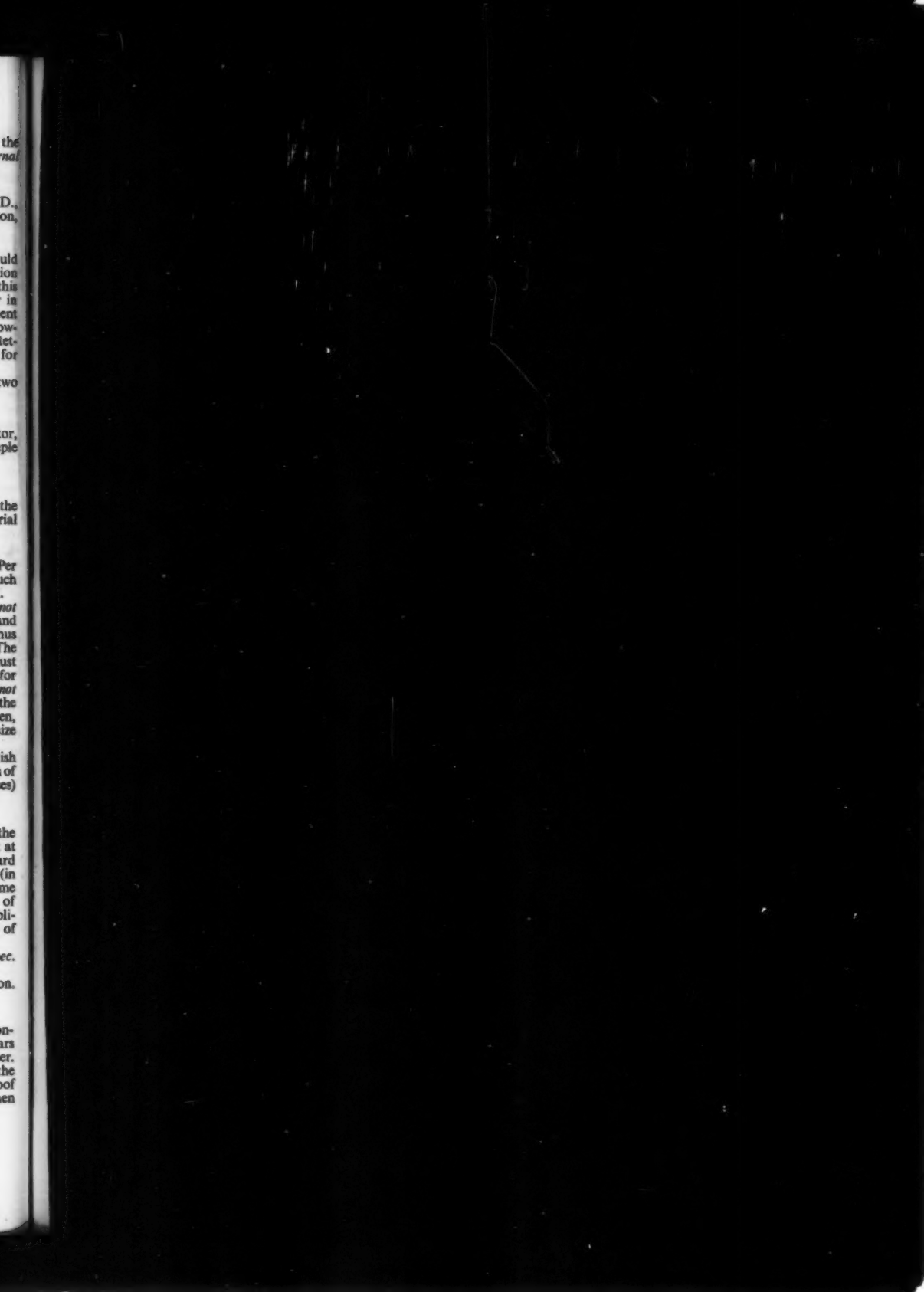
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